Desalination and Water Treatment
www.deswater.com

doi: 10.5004/dwt.2020.25754

191 (2020) 332–341
July

Gamma and UV radiation induced degradation of methotrexate (anti-rheumatic drug) in aqueous solution and conditions optimization

Muhammad Imran Kanjal[a], Majid Muneer[a,*], Ijaz Ahmad Bhatti[b], Muhammad Saeed[a], Atta-ul-Haq[a], Nighat Zia Ud Den[c], Ehsan ul Haq[d], Jan Nisar[e], Munawar Iqbal[f,*]

[a]*Department of Chemistry, Government College University Faisalabad 38000, Pakistan, emails: majid.chemist@yahoo.com (M. Muneer), imrankanjal786@gmail.com (M.I. Kanjal), pksaeed2003@yahoo.com (M. Saeed), attaulhaq@gcuf.edu.pk (Atta-ul-Haq)*
[b]*Department of Chemistry, University of Agriculture Faisalabad 38000, Pakistan, email: ijazchem@yahoo.com (I.A. Bhatti)*
[c]*Department of Biochemistry, Government College University Faisalabad 38000, Pakistan, email: nighatzia16@gmail.com (N.Z.U. Den)*
[d]*Pakistan Council for Scientific and Industrial Research (PCSIR) Lahore 54000, Pakistan, email: ehsanpcsir@gmail.com (E. ul Haq)*
[e]*National Center of Excellence in Physical Chemistry, University of Peshawar, Peshawar, 25120, Pakistan, email: pashkalawati@gmail.com (J. Nisar)*
[f]*Department of Chemistry, The University of Lahore, Lahore 53700, Pakistan, emails: munawar.iqbal@chem.uol.edu.pk/bosalvee@yahoo.com (M. Iqbal)*

Received 21 October 2019; Accepted 12 February 2020

ABSTRACT

Ionizing radiation-induced degradation of methotrexate (MTX) was carried out by UV and gamma-ray in combination with H_2O_2 (0.5 mL/L) as a function dose. The γ radiation dose, UV irradiation time, H_2O_2 dose and initial concentration of MTX were optimized and efficiency was evaluated based on degradation and chemical oxygen demand (COD) removal. The MTX removal efficiency (G-value), dose constant (k), $D_{0.5}$, $D_{0.9}$, and $D_{0.99}$ were calculated for γ-ray treatment. The MTX degradation was 78.17% and 86.62% when treatment was performed with 90 min UV exposure alone and in the presence of H_2O_2 (oxidant), whereas γ and γ/H_2O_2 furnished up to 93.66% and 99% degradation of MTX for the absorbed dose of 4 kGy. The COD reduction was 65% and 80% for UV/H_2O_2 and gamma/H_2O_2, respectively. The MTX degradation progress was monitored by high-performance liquid chromatography, Fourier-transform infrared spectroscopy and gas chromatography-mass spectrometry and results revealed that MTX was degraded efficiently by UV and γ radiation. The treatment could be used for the degradation of wastewater containing anti-rheumatic drugs.

Keywords: Methotrexate; Adsorbed dose; G-value; Ionizing radiation; Hydrogen peroxide; COD removal

1. Introduction

The methotrexate (MTX, 4 amino-N10-methylpteroylglutamic acid) has been used to cure lymphoblastic leukemia, non-hodking lymphoma and cancer/cerebral tumors. MTX has various adverse effects such as marrow suspension and ulcer etc. This drug has incomplete/partial absorption inside the body and excreted to environment, resulted soil, air and water contamination [1–4]. The MTX present in the surface water have challenging physical and chemical effects for the natural environment remediation and thus impose dangers to human health upon chronic exposure. These properties include sever toxicity, less biodegradability and recalcitrant character. The long term usage of water having traces of MTX, the drug incorporated in the human body and deposit in fatty tissues of organs and increase the risks of diseases

---

* Corresponding authors.

ultimately. The conventional water treatment methods such as coagulation, chlorination, adsorption etc. face certain problems for the treatment of wastewater [5–12]. The disadvantages include high cost, energy requirements, maintenance and disposal of the sludge waste [13–18]. The advanced oxidation processes (AOPs) is believed to be highly efficient for the degradation of drugs containing wastewater. The hydroxyl radical ($^{\bullet}$OH) generated by AOPs could be used to degrade the organic compounds via oxidative process having less chance of toxic by-products [7,19–21]. During the radiolysis, various kinds of radicals and ions are generated. These reactive species include hydroxyl radicals ($^{\bullet}$OH), hydrated electrons (e^-_{aq}), hydrogen radical ($H^{\bullet}$) play an important role during the decomposition of organic matter [10,22,23]. As a strong oxidizing agent, hydrogen peroxide (H_2O_2) promote the AOP to degrade the wastewater. During AOP, hydroxyl radicals ($^{\bullet}$OH) not only scavenge the e^-_{aq} and $H^{\bullet}$ but also promote the production of $^{\bullet}$OH (Eqs (1)–(3)). As a result, the hybrid process of gamma/H_2O_2 shows the synergetic effect by promoting the degradation of organic contaminants [23,24].

$$H_2O \xrightarrow{\gamma} {}^{\bullet}OH\left(0.29\right) + H^{\bullet}\left(0.06\right) + e^-_{aq}\left(0.28\right) + H_2\left(0.47\right) + H_2O_2\left(0.07\right) + H_3O^+\left(0.27\right) \quad (1)$$

$$H_2O_2 + e^-_{aq} \rightarrow {}^{\bullet}OH^+ - OH \quad (2)$$

$$H_2O_2 + {}^{\bullet}OH \rightarrow {}^{\bullet}OH + H_2O \quad (3)$$

The AOP is an innovative and effective method to degrade the complex organic compounds into simpler and less toxic molecules. The ionizing radiations have successfully been employed to degrade the wastewater, which resultantly reduced the toxic nature of complex molecule and improved the water quality parameters [25–27].

Based on aforementioned facts, MTX drug (Fig. 1) was treated by gamma and UV radiation alone and then in conjunction with oxidant (H_2O_2). The treatment efficiency was monitored on the basis of MTX degradation and chemical oxygen demand (COD) reduction as a function of γ ray absorbed dose, UV irradiation exposure time, H_2O_2 concentration and MTX initial concentration. The other parameters such as dose constant (k), $D_{0.50}$ (Dose required for 50% degradation), $D_{0.90}$ (Dose required for 90% degradation), $D_{0.99}$ (Dose required for 99% degradation) and removal efficiency (G-value) were determined for gamma-ray treated samples. The analytical techniques such as high-performance liquid chromatography (HPLC), Fourier-transform infrared spectroscopy (FTIR) and gas chromatography-mass spectrometry (GC-MS) were used to elucidate and identify radiolytic degradation by-products.

2. Material and methods

2.1. Reagents and chemicals

The commercial drug, MTX (molecular formula $C_{20}H_{22}N_8O_5$, purity 99%, molecular mass 454.447 g/mol, λ_{max} 372 nm, solubility 2,600 mg/L) was provided by the Pharmedic Laboratories Pvt. Ltd., Lahore, Pakistan. The solvents for mobile phase including acetonitrile and methanol (≥99.8 %) of HPLC grade were purchased from Tedia Company, USA. Acetic acid (99.5%) was purchased from BDH Limited Pool England, UK. The H_2O_2 was supplied by Scherlu, Germany.

2.2. Experimental setup

The drug solutions having concentration 5, 10, and 15 mg/L were treated with UV and UV/H_2O_2 for 15, 30, 45, 60, 75, and 90 min (UV lamps emitting radiations of fixed 254 nm wavelength and the intensity was 144 watt). For gamma ray treatment, Cs-137 gamma radiation source installed at Nuclear Institute for Agriculture and Biology (NIAB), Faisalabad, Pakistan was used. The calibration of source was carried out using Fricke dosimeter Eq. (4) and dose rate was 1.25 kGy h^{-1} at the time of irradiation of the samples.

$$D = \left[\frac{N \times \Delta A \times 100}{\varepsilon \times \rho \times G\left(\text{Fe}\left(\text{III}\right)\right)}\right] \quad (4)$$

Where, D is absorbed dose, ε is the molar extinction coefficient of ferric ion (0.2205 M^{-1} cm^{-1}) at 304 and 25°C, ΔA is representing the difference in absorbance of irradiated and un-irradiated samples, N is Avogadro's number, ρ is the density of Fricke solution (1.024 g/cm^3) and G (Fe^{+3}) is the number of Fe^{+3} ions produced/100 eV of absorbed energy.

2.3. Measurement of removal efficiency (G), $D_{0.50}$, $D_{0.90}$ and $D_{0.99}$ values

Eq. (5) was used to calculate the G-value of the drug aqueous solution treated with gamma radiation absorbed dose ranges 0.3 to 4 kGy [23].

$$G = \left[R\right]\frac{N_A}{D}\left(6.24 \times 10^{17}\right) \quad (5)$$

where R is the concentration of drug solution (mmol/L) at given dose, D is the absorbed dose in kGy, 6.24×10^{17} is the conversion factor from 100 eV/L and N_A is the Avogadro's number. The dose constant K is the slope of the plot of ln[R] vs. dose (kGy). $D_{0.5}$, $D_{0.9}$, and $D_{0.99}$ values were calculated using relations shown in Eqs. (6)–gv(8).

$$D_{0.5} = \ln 2/k \quad (6)$$

$$D_{0.9} = \ln 10/k \quad (7)$$

$$D_{0.99} = \ln 100/k \quad (8)$$

2.4. Analysis

The maximum absorbance at a particular wavelength (λ_{max}) of drug solutions and then change in absorbance at λ_{max} were measured by UV/Vis Spectrophotometer (U-2001 Hitachi, Japan) at Department of Chemistry, Government College University Faisalabad, Pakistan.

The HPLC system (Jasco PU-980 intelligent HPLC pump) was used for analysis. UV detector (303 nm), Rehodyne Model 7125 injector with a 20 μl sample loop and eluents

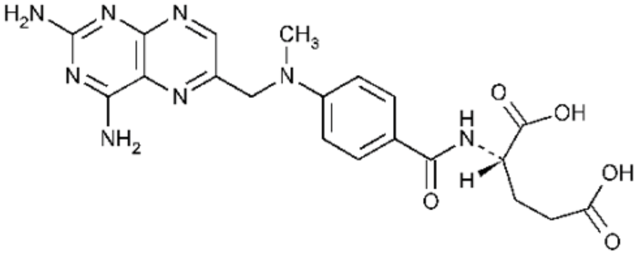


Fig. 1. Chemical structure of methotrexate drug.

were monitored by Jasco MD 910 Multi-wavelength Detector (DAD) connected to a computer station. The experimental conditions were optimized on the use of column HSA chiral C18 (250 mm × 4.6 mm, 5 µm) and different percentages (0.1%, 0.2%, 1.0%, and 2.0%) of acetic acid and triethylamine in the presence of 100% methanol were used as mobile phase with the flow rate of 0.8 ml/min. The buffer solution was prepared by dissolving 2.0 ml trimethylamine in water; glacial acetic acid was added to adjust the appropriate pH value before bringing the volume to 200 ml at Sayban Pharmaceuticals Pvt., Lahore, Pakistan.

The GC-MS analysis was performed in order to identify the degraded products. Prior to analysis, the irradiated samples were extracted with ethyl acetate. The organic phases were decanted followed by dehydration with $MgSO_4$ for 24 h. Then, samples were concentrated by rotatory vacuum evaporator and stored for analysis. The GC (Agilent Technologies 6890N, Santa Clara, CA 95051, United States) having DB-5 capillarycolumn coupled with MS detector through EIinterface using Helium as a carrier gas. The m/e ratios of fragments were determined by Chem. Station software and the identified compounds were then compared with software library at Pakistan Council of Scientific and Industrial Research (PCSIR) Lahore, Pakistan.

The FTIR analysis was performed in order to identify the change in the functional groups before and after treatment [28–36]. The organic extracts were evaporated and mixed with KBr powder and uniform disk was performed and analyzed by FTIR (Schimadzu U-2001 Japan) [37] at Central Hi-Tech Lab, Department of Chemistry, Government College University Faisalabad, Pakistan.

3. Results and discussion

3.1. Degradation by gamma radiation

Gamma ray induced degradation of MTX in aqueous media at various absorbed dosed in the presence of H_2O_2 is shown in Fig. 2. The MTX solution in aqueous media having concentration 5 to 15 mg/L was subjected to gamma radiation. The degradation efficiency improved with the increase of gamma ray absorbed dose due to the enhancement of reactive species ($^{\bullet}OH$) generated during the radiolysis of water resulting the decomposition of organic compounds [23]. The percentage degradation efficiency was observed up to 93.66%, 88.13%, and 87.37% for 5, 10, and 15 mg/L for 4 kGy gamma ray absorbed dose and degradation efficiency of MTX was noted as 99%, 94.38%, and 88.89% when the gamma treatment was performed in the presence of H_2O_2 (Figs. 2 and 3). The rate of the reaction is the change in concentration per energy. It has been observed that the radiation induced degradation follow the pseudo first order kinetics, which was calculated as shown in Eqs. (9)–(10).

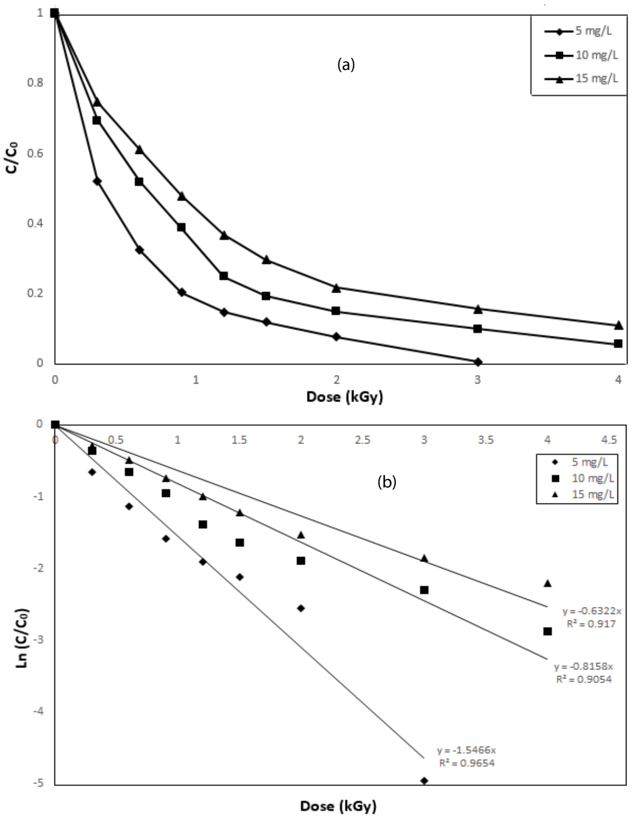


Fig. 2. (a) C/C_0 and (b) $\ln C/C_0$ vs. gamma radiation absorbed dose.

$$C = C_0 e^{-dD} \tag{9}$$

$$-\ln\left(\frac{C}{C_0}\right) = dD \tag{10}$$

where C_0 and C are the concentrations of MTX before and after treatment, respectively, d is the dose constant; D is absorbed dose. It was observed that 99% MTX degradation was achieved using 5 mg/L initial concentration at the gamma radiation absorbed dose of 4 kGy in the presence of H_2O_2. The absorbance at λ_{max} attributed to radiation induced degradation of MTX followed by splitting the complex compounds into simpler molecules [26]. The degradation rate was significantly enhanced in the presence of H_2O_2. The gamma/H_2O_2 produce hydroxyl radicals ($^{\bullet}OH$) which not only scavenge the e^-_{aq} and $H^{\bullet}$ but also promote the production of $^{\bullet}OH$ (Eqs. (1)–(3)) resulting significant enhancement in the degradation. These results are in agreement with previous studies for NPEO (Nonylphenol ethoxylate) [23] and wastewater [26]. The response surface methodology proves the effectiveness of the treatment method and shows the complete degradation by using the gamma/H_2O_2 hybrid process (Fig. 4).

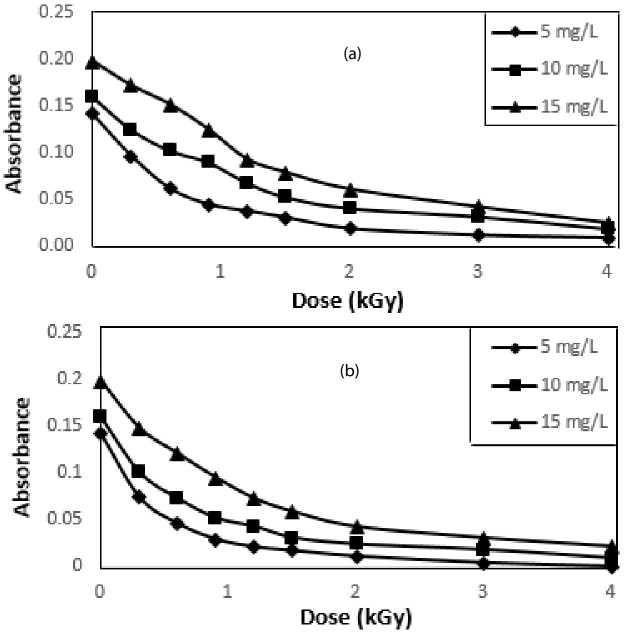


Fig. 3. (a) Methotrexate degradation (absorbance) as a function of gamma radiation absorbed dose and (b) methotrexate degradation (absorbance) as a function of gamma radiation absorbed dose in the presence of H_2O_2.

3.2. Degradation by UV radiation

The MTX was subjected to UV radiation for 15, 30, 45, 60, 75, and 90 min. The percentage degradation was recorded as 23.24%, 49.30%, 63.38%, 71.13%, 74.65%, and 78.17% for 5 mg/L, whereas 19.38%, 30.63%, 39.38%, 50.63%, 29.38%, and 69.36% for 10 mg/L and 10.10%, 17.68%, 30.81%, 44.95%, 53.54%, and 60.61% for 15 mg/L (Figs. 5 and 6). The UV radiation along with H_2O_2 based AOP generates hydroxyl radicals ($^\bullet OH$) and many researchers revealed the potency of the UV/H_2O_2 combined method to degrade the antibiotics [38]. Here, degradation was observed to be 26.06%, 54.23%, 68.31%, 75.35%, 80.99%, and 86.62% for 5 mg/L, 21.88%, 43.45%, 53.13%, 65.63%, 73.75%, and 80.63% for 10 mg/L while 16.67%, 28.28%, 44.95%, 50.51%, 61.11%, and 73.23% for 15 mg/L. It was observed that as the UV radiation exposure time increased, the percentage degradation also increased and maximum degradation was achieved at UV exposure time 90 min. Beyond this, no degradation was observed because of the competition between intermediate species, the $^\bullet OH$ radical and converted into hydroperoxyl radical $HO_2^\bullet$and process efficiency may reduce as the H_2O_2 exceeds from optimum amount, it scavenges $^\bullet OH$ and ultimately, the degradation may decreased [26]. A similar trend was discussed by Jung et al. [39], who degraded Amoxicillin antibiotic using UV/H_2O_2 advanced oxidation.

3.3. COD removal efficiency

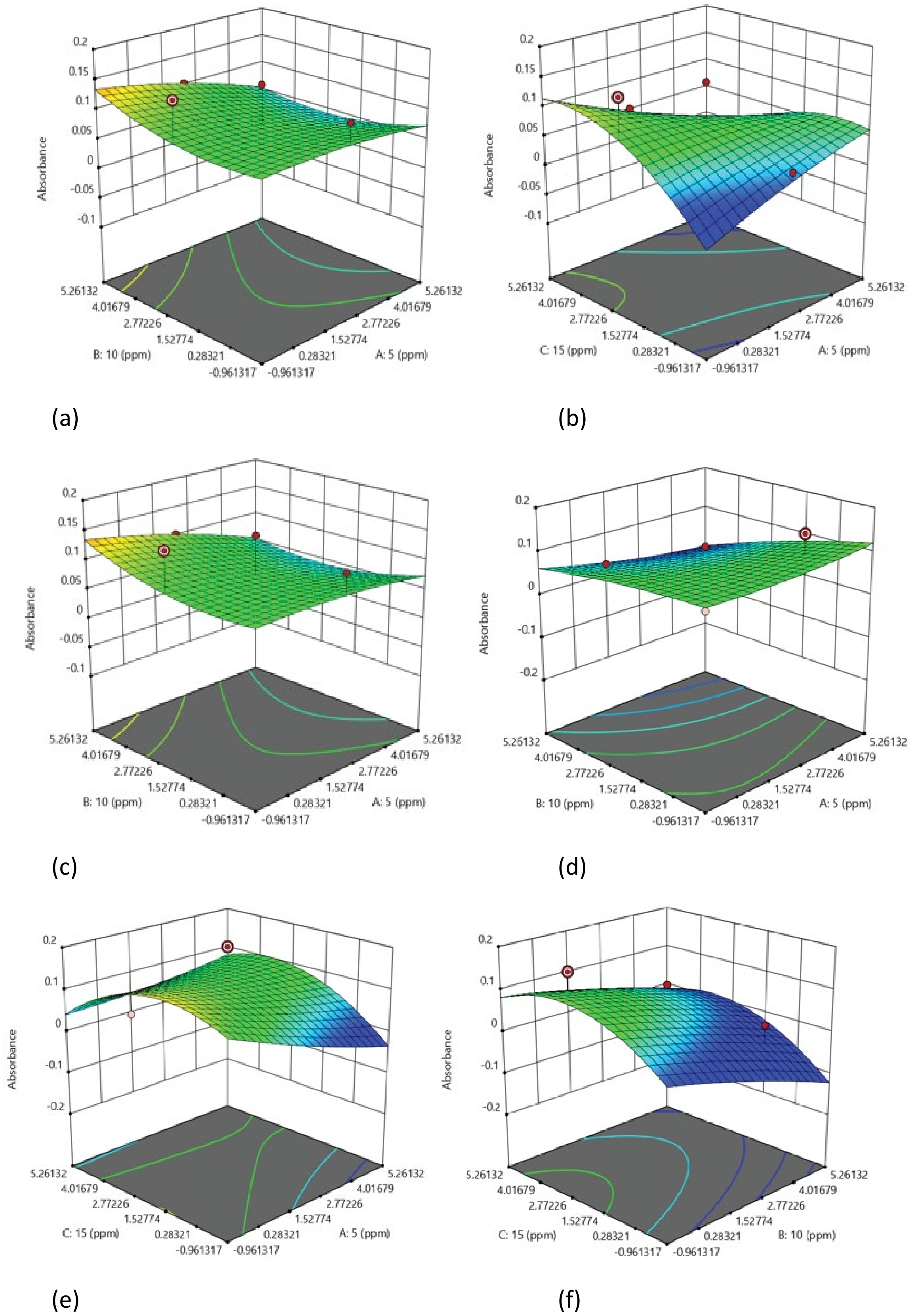
The percentage reduction of COD for the gamma radiation absorbed doses that is, 0.3, 0.6, 0.9, 1.2, 1.5, 2, 3, and 4 kGy were recorded to be 26%, 34%, 42%, 48%, 56%, 64%, 69%, and 73% for 5 mg/L and 18%, 28%, 35%, 42%, 48%, 56%, 64%, and 68% for 10 mg/L and 12%, 19%, 25%, 32%, 41%, 49%, 57%, and 67% for 15 mg/L (Fig. 6a). The gamma/H_2O_2 was more efficient and effective for the reduction in COD since hydrogen peroxide interact with hydrated electron (e^-_{aq}) and hydrogen radicals ($H^\bullet$) to scavenge them. In fact, the oxidative degradation occurs by hydroxyl radicals produced during the radiolysis is facilitated in the presence of H_2O_2 [40]. The percentage removal of COD values were 29%, 39%, 48%, 57%, 63%, 68%, 74%, and 81% for 5 mg/L and 22%, 32%, 39%, 47%, 51%, 60%, 69%, and 76% for 10 mg/L while 15%, 25%, 31%, 39%, 43%, 49%, 57%, and 68% for 15 mg/L using gamma/H_2O_2 treatment (Fig. 6b). The COD removal for the UV radiation treatment was also investigated and the percentage reduction of COD were 17%, 25%, 38%, 45%, 51%, and 57% for 5 mg/L, 12%, 19%, 31%, 39%, 44%, and 51% for 10 mg/L and 9%, 15%, 27%, 33%, 38%, and 47 % for 15 mg/L for 15, 30, 45, 60, 75, and 90 min irradiation time, respectively (Fig. 7a). A significant reduction in COD was observed for UV/H_2O_2 that were 25%, 34%, 43%, 49%, 59%, and 68% for 5 mg/L, 19%, 27%, 35%, 43%, 53%, and 62% for 10 mg/L, 15%, 24%, 31%, 39%, 47%, and 55% for 15 mg/L, respectively (Fig. 7b). It was observed that COD removal was increased linearly with gamma radiation absorbed dose. Being high energy radiation, gamma radiation degrade the complex organic compounds into simpler molecules resulting the reduction in COD as it is measure of oxygen consumed during the decomposition of organic matter. Our results were in correlation with the study of Iqbal et al. [26] who degraded the industrial wastewater photo-catalytically and observed the reduction in COD which indicated that the organic contents in the system decreased.

3.4. Gamma ray treatment efficiency

The radiolytic degradation efficiency was evaluated by measuring the removal efficiency (*G*-value), $D_{0.50}$, $D_{0.90}$ and $D_{0.99}$ of gamma ray treated samples and responses thus obtained are shown in Tables 1 and 2 and Fig. 8. The values of $D_{0.50}$, $D_{0.90}$, and $D_{0.99}$ increased with the increase in concentration of MTX because gamma ray absorbed dose required to degrade the sample 50%, 90%, and 99%, enhanced by increasing the concentration [23,26]. The *G*-value was decreased with the concentration, it is because of that the competition between reaction intermediate and some reactive species and thus more dose of gamma radiation is required at higher concentration of the drug [18,27]. As mentioned in Table 2 that in the presence of H_2O_2 the radiolytic degradation efficiency was increased and low dose is required to remove 50%, 90%, and 99% MTX.

3.5. MTX radiolytic by-product monitoring

The aqueous solution of MTX was subjected to gamma and UV radiations and degradation was studied with the help of HPLC (Fig. 9a). It was observed that when the sample were treated with UV and gamma radiation, the peak area was decreased. Similarly, the peak area was more prominent when the samples were treated with UV and gamma radiation in the presence of H_2O_2. Also, GC-MS was performed in order to study the degradation of the MTX drug and to identify the degraded end products. Due to



(a) (b) (c) (d) (e) (f)

Fig. 4. Response surface plots (a–c) showing the effect of gamma radiation on the absorbance of methotrexate while (d–f) gamma along with H_2O_2

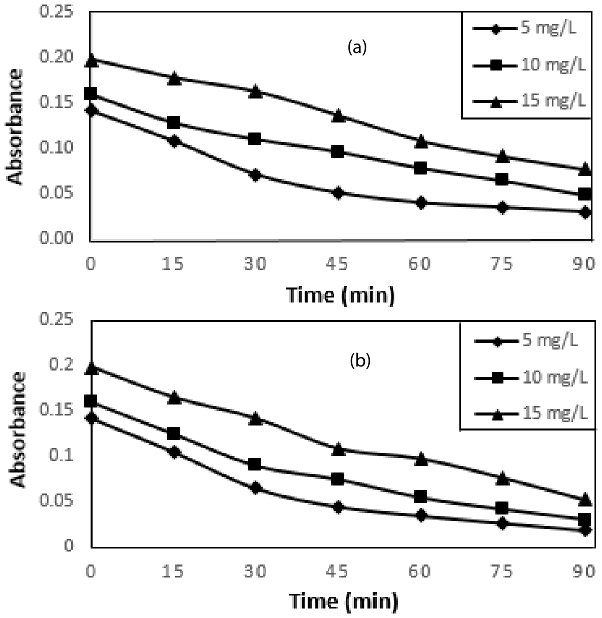


Fig. 5. (a) Methotrexate degradation (absorbance) as a function of UV irradiation time and (b) methotrexate degradation (absorbance) as a function of UV irradiation time in the presence of H_2O_2.

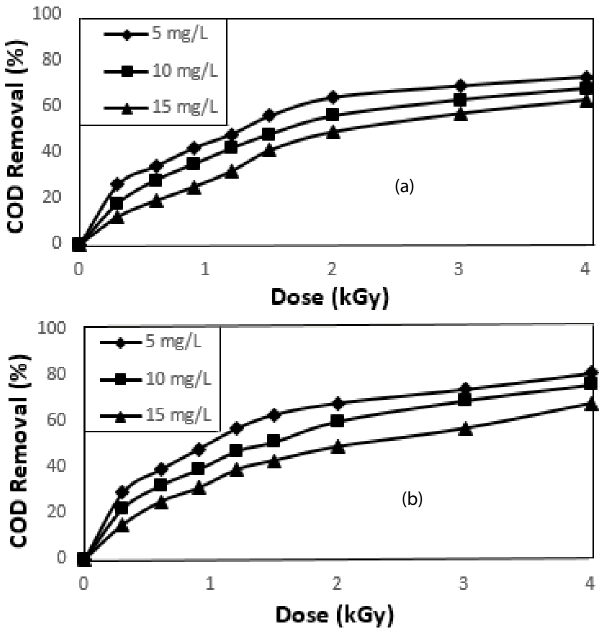


Fig. 6. (a) COD removal of MTX by gamma radiation and (b) COD removal of MTX by gamma radiation in the presence of H_2O_2.

heterolytic cleavage of C-N bond between *p*-methylaminobenzoyl and diaminopteridinemethylene, the fragment with m/z 308.1261 give raise the segment ions with m/z 134.0546 and 175.0659 finally degraded to CO_2 and H_2O (Scheme 1). There was significance decrease in peaks and the decrease was more prominent when the samples were treated with

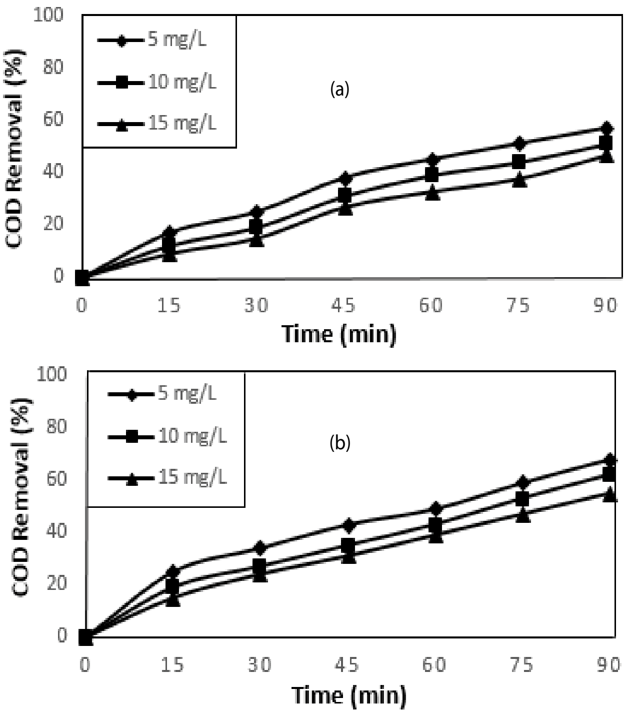


Fig. 7. (a) COD removal of MTX by UV and (b) COD removal of MTX by UV in the presence of H_2O_2.

Table 1
Gamma radiation efficiency for the removal of methotrexate

Conc. (mg/L)	Dose (kGy)	*G*-Value	
5	0.3	0.11221	
	0.6	0.04361	
	0.9	0.01413	$D_{0.50}$ = 1.0178
	1.2	0.00435	$D_{0.90}$ = 3.3811
	1.5	0.00349	$D_{0.99}$ = 6.7623
	2	0.00548	K = 0.681
	3	0.00174	R^2 = 0.936
	4	0.00056	
10	0.3	0.15490	
	0.6	0.04867	
	0.9	0.01916	$D_{0.50}$ = 1.3322
	1.2	0.01433	$D_{0.90}$ = 4.4254
	1.5	0.01328	$D_{0.99}$ = 8.8509
	2	0.00796	K = 0.520
	3	0.00397	R^2 = 0.97
	4	0.00231	
15	0.3	0.13947	
	0.6	0.05363	
	0.9	0.04828	$D_{0.50}$ = 1.4225
	1.2	0.04290	$D_{0.90}$ = 4.4934
	1.5	0.01502	$D_{0.99}$ = 8.9868
	2	0.01447	K = 0.5241
	3	0.01019	R^2 = 0.987
	4	0.00683	

Table 2
Gamma radiation efficiency for the removal of methotrexate in the presence of H_2O_2

Conc. (mg/L)	Dose (kGy)	*G*-Value	
5	0.3	0.16956	$D_{0.50}$ = 1.019484 $D_{0.90}$ = 3.386653 $D_{0.99}$ = 6.773305 K = 0.6799 R^2 = 0.684
	0.6	0.03490	
	0.9	0.01411	
	1.2	0.00499	
	1.5	0.00199	
	2	0.00124	
	3	0.00104	
	4	0.00074	
10	0.3	0.26110	$D_{0.50}$ = 1.047842 $D_{0.90}$ = 3.480854 $D_{0.99}$ = 6.961708 K = 0.6615 R^2 = 0.941
	0.6	0.06195	
	0.9	0.03096	
	1.2	0.00996	
	1.5	0.00866	
	2	0.00460	
	3	0.00247	
	4	0.00112	
15	0.3	0.26818	$D_{0.50}$ = 1.265098 $D_{0.90}$ = 4.202565 $D_{0.99}$ = 8.405129 K = 0.5479 R^2 = 0.955
	0.6	0.07242	
	0.9	0.04649	
	1.2	0.02948	
	1.5	0.01502	
	2	0.01287	
	3	0.00643	
	4	0.00362	

gamma radiation absorbed dose with 4 kGy in the presence of H_2O_2 and no characteristics peak was appeared, which shows that complete degradation was achieved at 4 kGy/H_2O_2 (Fig. 9b).

The FTIR profile of untreated MTX reveled the characteristic absorptions band at 3,400 cm^{-1} (O–H stretching from carboxyl groups superposed with the O–H stretching), primary amine N–H stretching was found at 3,050 cm^{-1}, while C=O stretching was observed at 1,720 cm^{-1} in which C=O appeared from the amidic group and –C=O from carboxylic group. The above data indicates the splitting of the C=O into two peaks in the MTX. The aromatic –C=C stretching was overlapped by a spectral range of 1,500–1,480 cm^{-1} which was a band corresponding to N–H bending appeared from amidic group. The FTIR spectrum of irradiated MTX at 4 kGy radiation absorbed dose has significant variations as compared to un-irradiated MTX. The complete destruction of aromatic rings occurs after radiation treatment but some minor peak appeared at 2,980 cm^{-1} was attributed to CH stretching and at 1,216 cm^{-1} a peak corresponds to –CO stretching while other peaks disappeared due to elimination of characteristics vibration (Fig. 10). FTIR of treated samples clearly indicate that MTX molecules have been degraded which support the assumption that $^•OH$ bring about the chain oxidation reaction to break down dye molecule via destruction of aromatic rings and N–N and finally into CO_2 and water [23,25,26,41]. The UV and gamma radiation induced degradation of MTX is proved to highly efficient, which can be utilized for the degradation of MTX in wastewater and in view of current scenario of environmental pollution [1,4,9,13,14,42–54], there is a need to develop efficient methods for wastewater treatment and AOPs are proved to be potential in this regard [55].

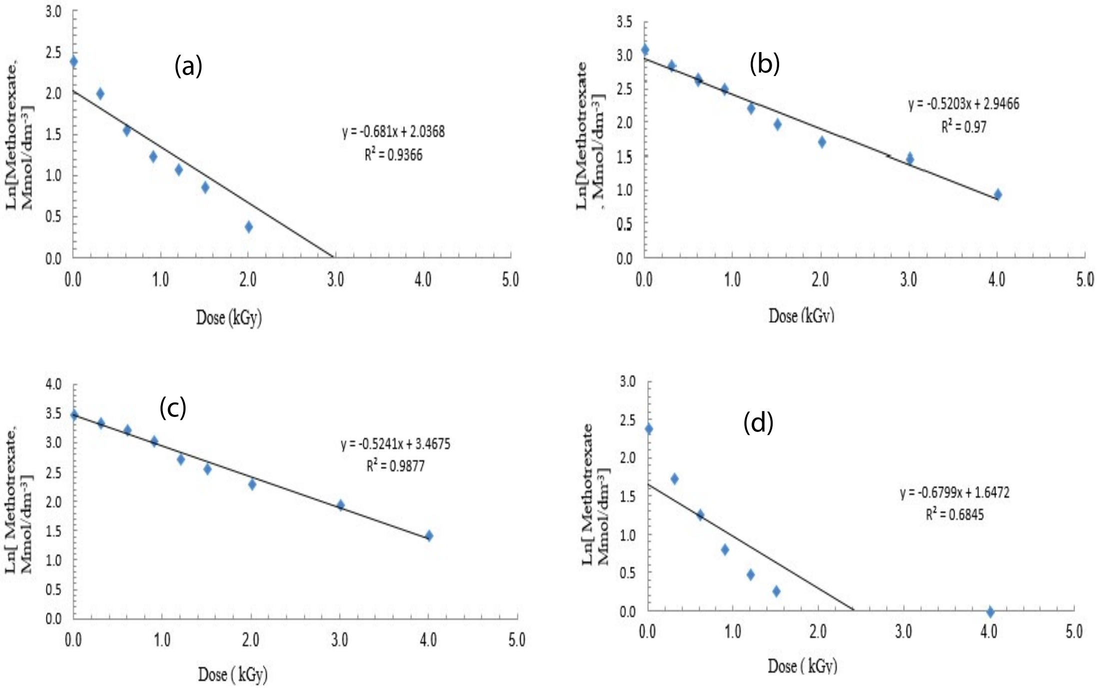


Fig. 8. Continued

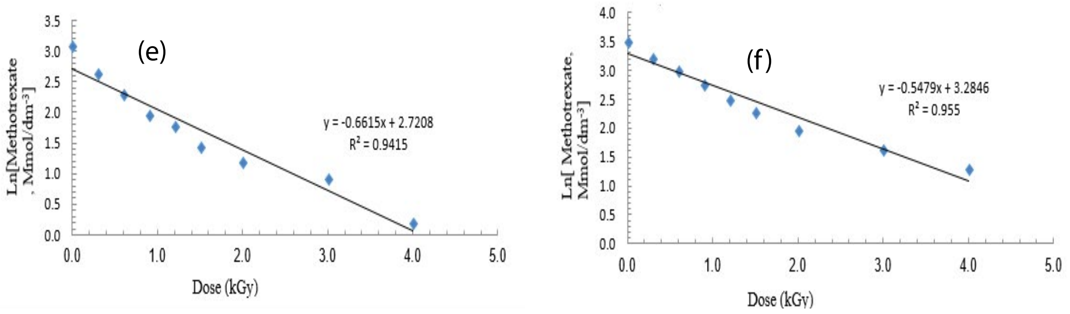


Fig. 8. Gamma radiation removal efficiency of methotrexate (a) 5 mg/L without H_2O_2, (b) 10 mg/L without H_2O_2, (c) 15 mg/L without H_2O_2, (d) 5 mg/L with H_2O_2, (e) 10 mg/L with H_2O_2, and (f) 15 mg/L with H_2O_2.

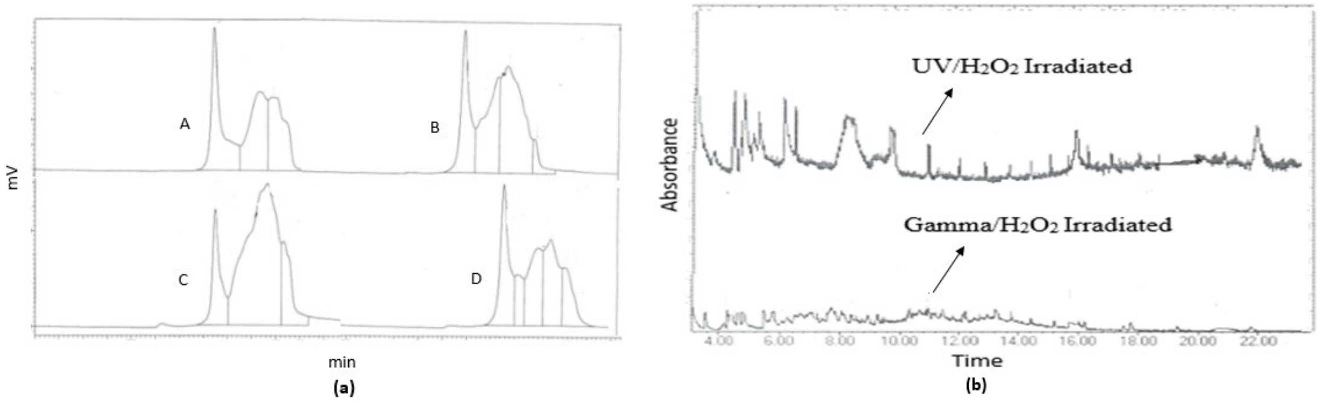


Fig. 9. (a) HPLC chromatogram of methotrexate (A) UV, (B) UV/H_2O_2, (C) Gamma, (D) $Gamma/H_2O_2$, and (b) GC-MS profile of methotrexate treated by UV and gamma radiation.

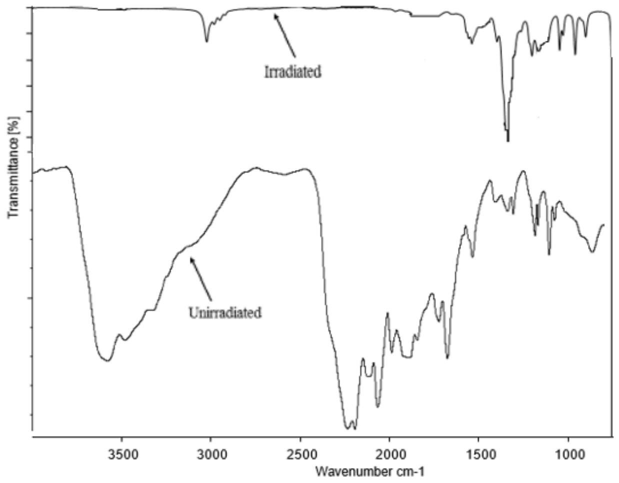
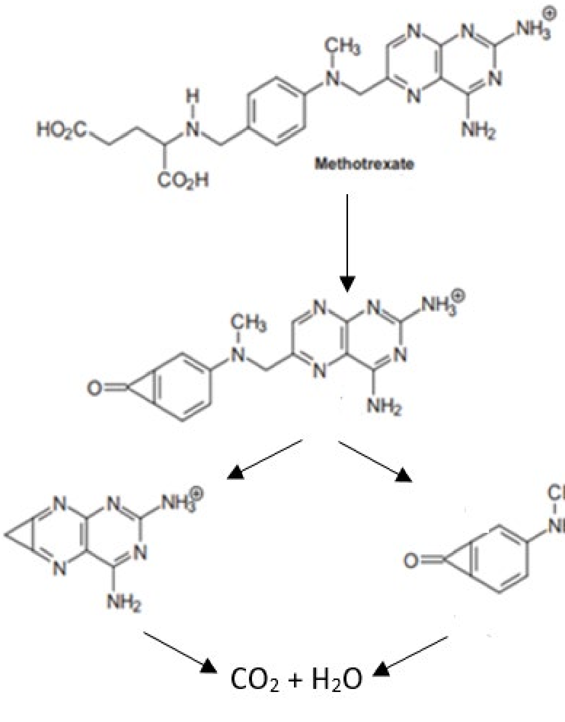


Fig. 10. FTIR profile of methotrexate before and after treatment.

4. Conclusion

The degradation of MTX by UV and gamma radiation along with H_2O_2 was evaluated. The complete degradation of MTX was found by employing gamma/H_2O_2 hybrid process with a significant reduction in COD value. The results of FTIR, HPLC and GC-MS support the theoretical



Scheme. 1. Proposed degradation pathways of methotrexate.

degradation pathway and revealed that no peak appeared after gamma/H_2O_2 treatment verifying the complete degradation. The obtained data in the current project suggests that wastewater containing drug can efficiently be treated usingAOPs based on gamma radiation coupled with H_2O_2.

Acknowledgment

The authors are thankful to the authorities of Pharmedic Laboratories (Pvt) Lahore to provide "Methotrexate" drug. The analytical services provided by the Sayban Pharmaceutical (Pvt) Lahore and Pakistan Council of Science and Industrial research (PCSIR) Lahore are also acknowledged.

References

[1] M.R. Boleda, K. Majamaa, P. Aerts, V. Gómez, M.T. Galceran, F. Ventura, Removal of drugs of abuse from municipal wastewater using reverse osmosis membranes, Desal. Water Treat., 21 (2010) 122–130.

[2] L.R. Rogers, Cerebrovascular Complications of Cancer, in: Cancer Neurology in Clinical Practice, Springer, 2018, pp. 171–191.

[3] K. Schmiegelow, Advances in individual prediction of methotrexate toxicity: a review, Br. J. Haematol., 146 (2009) 489–503.

[4] F. Naitali, H. Ghoualem, Becoming of pharmaceutical rejections in urban wastewater, Desal. Water Treat., 52 (2014) 2340–2343.

[5] D. Husaain, M. Najam-ul-Haq, A. Saeed, F. Jabeen, M. Athar, M. Naeem ashiq, Synthesis of poly GMA/DVB and its application for the removal of Malachite Green from aqueous medium by adsorption process, Desal. Water Treat., 53 (2015) 2518–2528.

[6] S. Giri, P. Sahoo, R. Das, N. Das, Coke/Fe_3O_4 nanoparticle composites: synthesis, characterization and adsorption behaviour towards organic dyes, Desal. Water Treat., 57 (2016) 17483–17493.

[7] M. Saeed, S. Adeel, M. Ilyas, M.A. Shahzad, M. Usman, E.-u. Haq, M. Hamayun, Oxidative degradation of Methyl Orange catalyzed by lab prepared nickel hydroxide in aqueous medium, Desal. Water Treat., 57 (2016) 12804–12813.

[8] G. Abbas, I. Javed, M. Iqbal, R. Haider, F. Hussain, N. Qureshi, Adsorption of non-steroidal anti-inflammatory drugs (diclofenac and ibuprofen) from aqueous medium onto activated onion skin, Desal. Water Treat., 95 (2017) 274–285.

[9] A.M. Awwad, N.M. Salem, M.M. Aqarbeh, F.M. Abdulaziz, Green synthesis, characterization of silver sulfide nanoparticles and antibacterial activity evaluation, Chem. Int., 6 (2020) 42–48.

[10] M. Muneer, S. Adeel, S. Ayub, M. Zuber, F. Ur-Rehman M.I. Kanjal, M. Iqbal, M. Kamran, Dyeing behavior of microwave assisted surface modified polyester fabric using Disperse Orange 25: improvement in color strength and fastness properties, Oxid. Commun., 2 (2016) 1430.

[11] F. Minas, B.S. Chandravanshi, S. Leta, Chemical precipitation method for chromium removal and its recovery from tannery wastewater in Ethiopia, Chem. Int., 3 (2017) 392–405.

[12] A.O. Majolagbe, A.A. Adeyi, O. Osibanjo, A.O. Adams, O.O. Ojuri, Pollution vulnerability and health risk assessment of groundwater around an engineering Landfill in Lagos, Nigeria, Chem. Int., 3 (2017) 58–68.

[13] M.M. Alaqarbeh, M.W. Shammout, A.M. Awwad, Nano platelets kaolinite for the adsorption of toxic metal ions in the environment, Chem. Int., 6 (2020) 49–55.

[14] A.M. Alkherraz, A.K. Ali, K.M. Elsherif, Removal of Pb(II), Zn(II), Cu(II) and Cd(II) from aqueous solutions by adsorption onto olive branches activated carbon: equilibrium and thermodynamic studies, Chem. Int., 6 (2020) 11–20.

[15] A. Hamilton-Amachree, N.B. Iroha, Corrosion inhibition of API 5L X80 pipeline steel in acidic environment using aqueous extract of *Thevetia peruviana*, Chem. Int., 6 (2020) 117–128.

[16] C. Ukpaka, BTX degradation: the concept of microbial integration, Chem Int., 3 (2016) 8–18.

[17] N.K. Benabdallah, D. Harrache, A. Mir, M. de la Guardia, F.-Z. Benhachem, Bioaccumulation of trace metals by red alga Corallina elongata in the coast of Beni Saf, west coast, Algeria, Chem. Int., 3(2017) 220–231.

[18] S. Jafarinejad, Activated sludge combined with powdered activated carbon (PACT process) for the petroleum industry wastewater treatment: a review, Chem. Int., 3 (2017) 268–277.

[19] K. Qureshi, M.Z. Ahmad, I.A. Bhatti, M. Zahid, J. Nisar, M. Iqbal, Graphene oxide decorated $ZnWO_4$ architecture synthesis, characterization and photocatalytic activity evaluation, J. Mol. Liq., 285 (2019) 778–789.

[20] M. Zuber, S. Adeel, F.-U. Rehman, F. Anjum, M. Muneer, M. Abdullah, K.M. Zia, Influence of microwave radiation on dyeing of bio-mordanted silk fabric using neem bark (*Azadirachta indica*)-based tannin natural dye, J. Nat. Fibers, (2019) 1–13.

[21] M. Saeed, A. Haq, M. Muneer, S. Adeel, M. Hamayun, M. Ismail, M. Younas, Degradation of Direct Black 38 dye catalyzed by lab prepared nickel hydroxide in aqueous medium, Global Nest J., 18 (2016) 309–320.

[22] S.-S. Chang, S.O. Yoon, H.J. Park, A. Sakai, Luminescence properties of Zn nanowires prepared by electrochemical etching, Mater. Lett., 53 (2002) 432–436.

[23] M. Iqbal, I.A. Bhatti, Gamma radiation/H_2O_2 treatment of a nonylphenol ethoxylates: degradation, cytotoxicity, and mutagenicity evaluation, J. Hazard. Mater., 299 (2015) 351–360.

[24] M. Saeed, S. Adeel, M.A. Shahzad, Atta-ul-Haq, M. Muneer, M. Younas, Pt/Al_2O_3 catalyzed decolorization of rhodamine B dye in aqueous medium, Chiang Mai J. Sci., 42 (2015) 730–744.

[25] M. Iqbal, J. Nisar, Cytotoxicity and mutagenicity evaluation of gamma radiation and hydrogen peroxide treated textile effluents using bioassays, J. Environ. Chem. Eng., 3 (2015) 1912–1917.

[26] M. Iqbal, J. Nisar, M. Adil, M. Abbas, M. Riaz, M.A. Tahir, M. Younus, M. Shahid, Mutagenicity and cytotoxicity evaluation of photo-catalytically treated petroleum refinery wastewater using an array of bioassays, Chemosphere, 168 (2017) 590–598.

[27] A. Jamil, T.H. Bokhari, M. Iqbal, I.A. Bhatti, M. Zuber, J. Nisar, N. Masood, Gamma radiation and hydrogen peroxide based advanced oxidation process for the degradation of disperse dye in aqueous medium, Z. Phys. Chem., 234 (2019) 279–294.

[28] J. Bhuvana, G. Madhurambal, Effect of trytophan as dopant on potassium acid phthalate single crystals, Chem. Int., 1 (2015) 87–91.

[29] M. Pervaiz, K.M. Butt, M.A. Raza, A. Rasheed, S. Ahmad, A. Adnan, M. Iqbal, Extraction and applications of aluminum hydroxide from bauxite for commercial consumption, Chem. Int., 1 (2015) 99.

[30] R.D. El Bouzaidi, A. El Gridani, Study of the vibronic coupling in the ground state of Methylthio radical, Chem. Int., 2 (2016) 70–79.

[31] Y. Zhao, D. Wang, X. Li, Y. Liu, Determination of rutin, chlorogenic acid and quercetin in solidaginis by large volume sample stacking with polarity switching and acid barrage stacking, Chem. Int., 2 (2016) 121.

[32] K. Desta, M. Amare, Validated UV-Visible spectrometry using water as a solvent for determination of chloroquine in tablet samples, Chem. Int., 3 (2017) 288–295.

[33] A.H. Abubakar Siddique, S.R. Khan, A. Inayat, A. Nazir, M. Iqbal, Appraisal of heavy metals and nutrients from phosphate rocks, Khyber Pakhtunkhwa, Pakistan, Chem. Int., 4 (2018) 1–6.

[34] N.A. Ayofe, P.O. Oladoye, D.O. Jegede, Extraction and quantification of phthalates in plastic coca-cola soft drinks using high performance liquid chromatography (HPLC), Chem. Int., 4 (2018) 85–90.

[35] S. Gul, A. Hameed, UV spectroscopic method for determination of phenytoin in bulk and injection forms, Chem. Int., 4 (2018) 177–182.

[36] Y. Nikodimos, B. Hagos, D. Dereje, M. Hussen, Voltammetric study of secnidazole and its determination in pharmaceutical

tablet using 1, 4-benzoquinone modified carbon paste electrode, Chem. Int., 4 (2018) 43–51.

[37] Q. Bao, L. Chen, J. Tian, J. Wang, Degradation of 2-mercaptobenzothiazole in aqueous solution by gamma irradiation, Radiat. Phys. Chem., 103 (2014) 198–202.

[38] M. Muneer, N. Hafiz, M. Usman, F.U. Rehman, M. Saeed, H. Bhatti, M. Kanjal, Environmentally friendly oxidative degradation of reactive orange dye by high energy radiation, Oxid. Commun., 38 (2015) 2091–2099.

[39] Y.J. Jung, W.G. Kim, Y. Yoon, J.-W. Kang, Y.M. Hong, H.W. Kim, Removal of amoxicillin by UV and UV/H_2O_2 processes, Sci. Total Environ., 420 (2012) 160–167.

[40] M. Iqbal, M. Abbas, M. Arshad, T. Hussain, A.U. Khan, N. Masood, M.A. Tahir, S.M. Hussain, T.H. Bokhari, R.A. Khera, Gamma radiation treatment for reducing cytotoxicity and mutagenicity in industrial wastewater, Pol. J. Environ. Stud., 24 (2015) 2745–2750.

[41] S. Ata, I. Shaheen, S. Ghafoor, M. Sultan, F. Majid, I. Bibi, M. Iqbal, Graphene and silver decorated ZnO composite synthesis, characterization and photocatalytic activity evaluation, Diamond Relat. Mater., 90 (2018) 26–31.

[42] A. Sasmaz, I.M. Dogan, M. Sasmaz, Removal of Cr, Ni and Co in the water of chromium mining areas by using *Lemna gibba* L. and *Lemna minor* L, Water Environ. J., 30 (2016) 235–242.

[43] M. Sasmaz, B. Akgul, D. Yıldırım, A. Sasmaz, Bioaccumulation of thallium by the wild plants grown in soils of mining area, Int. J. Phytorem., 18 (2016) 1164–1170.

[44] M. Sasmaz, A. Sasmaz, The accumulation of strontium by native plants grown on Gumuskoy mining soils, J. Geochem. Explor., 181 (2017) 236–242.

[45] L.S. Al Banna, N.M. Salem, A.M. Awwad, Green synthesis of sulfur nanoparticles using *Rosmarinus officinalis* leaves extract and anti-nematicidal activity against *Meloidogyne javanica*, Chem. Int., 6 (2020) 137–143.

[46] S. Şaşmaz, S. Gedikli, P. Aytar, G. Güngörmedi, A. Çabuk, E. Hür, A. Ünal, N. Kolankaya, Decolorization potential of some reactive dyes with crude laccase and laccase-mediated system, Appl. Biochem. Biotechnol., 163 (2011) 346–361.

[47] M. Iqbal, M. Abbas, J. Nisar, A. Nazir, Bioassays based on higher plants as excellent dosimeters for ecotoxicity monitoring: a review, Chem. Int., 5 (2019) 1–80.

[48] I.A. Adetutu, G.N. Iwuoha, H. Michael Jnr, Carcinogenicity of dioxin-like polychlorinated biphenyls in transformer soil in vicinity of University of Port Harcourt, Choba, Nigeria, Chem. Int., 6 (2020) 144–150.

[49] E.B. Hassen, A.M. Asmare, Predictive performance modeling of Habesha brewery wastewater treatment plant using artificial neural networks, Chem. Int., 5 (2019) 87–96.

[50] C.P. Ukpaka, P.E. Uku, Application of mathematical tools and techniques in monitoring, predicting stainless steel corrosion in river water media environment, Chem. Int., 4 (2018) 77–84.

[51] S. Mansouri, N. Elhammoudi, S. Aboul-hrouz, M. Mouiya, L. Makouki, A. Chham, A. Abourriche, H. Hannache, M. Oumam, Elaboration of novel adsorbent from Moroccan oil shale using Plackett–Burman design, Chem. Int., 4 (2018) 7–14.

[52] S. Ghezali, A. Mahdad-Benzerdjeb, M. Ameri, A.Z. Bouyakoub, Adsorption of 2,4,6-trichlorophenol on bentonite modified with benzyldimethyltetradecylammonium chloride, Chem. Int., 4 (2018) 24–32.

[53] N.E. Ibisi, C.A. Asoluka, Use of agro-waste (*Musa paradisiaca* peels) as a sustainable biosorbent for toxic metal ions removal from contaminated water, Chem. Int., 4 (2018) 52–59.

[54] K. Djehaf, A.Z. Bouyakoub, R. Ouhib, H. Benmansour, A. Bentouaf, A. Mahdad, N. Moulay, D. Bensaid, M. Ameri, Textile wastewater in Tlemcen (Western Algeria): impact, treatment by combined process, Chem. Int., 3 (2017) 414–419.

[55] M.R. Bhuiyan, A. Shaid, M. Hossain, M.A. Khan, Decolorization and decontamination of textile wastewater by gamma irradiation in presence of H_2O_2, Desal. Water Treat., 57 (2016) 21545–21551.