Desalination and Water Treatment
www.deswater.com

doi: 10.5004/dwt.2017.20240

70 (2017) 339–346
April

Oxidative degradation of the antineoplastic drugs 5-fluorouracil and cytarabine in aqueous solution by potassium permanganate

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Received 18 May 2016; Accepted 26 September 2016

ABSTRACT

5-Fluorouracil (5-FU) and cytarabine (Ara-C) are two commonly used antineoplastic drugs, which are ecotoxic and genotoxic and frequently detected in hospital wastewater. Potassium permanganate ($KMnO_4$) has been widely used to remove organic pollutants from wastewater. The oxidative degradation of 5-FU and Ara-C in aqueous solution by $KMnO_4$ has not been reported. In this study, the oxidative degradation of 5-FU and Ara-C with $KMnO_4$ in aqueous solution was investigated. 5-FU was oxidized rapidly by $KMnO_4$ due to the olefinic group in the central heterocyclic ring. The degradation kinetics of 5-FU was well described by the equation of $-d[\text{5-FU}]/dt = k_{app}[\text{5-FU}]_t^{0.77}[KMnO_4]_t^{0.86}$. The degradation kinetics of Ara-C followed a generalized second-order rate law. The apparent rate constant (k_{app}) of these two target compounds was strongly depended on the reaction temperature, pH, humic acid (HA) and water quality. The apparent activation energies (E_a) of 5-FU and Ara-C were 32 and 40 $kJ\cdot mol^{-1}$, respectively, indicating that 5-FU was more easily decomposed by $KMnO_4$ as compared with Ara-C. The maximum values of k_{app} for 5-FU and Ara-C were 1.73×10^{-4} $\mu M^{-0.63}\cdot s^{-1}$ at pH 7.4 and 1.52 $M^{-1}\cdot s^{-1}$ at pH 3.5, respectively. The oxidative degradation of 5-FU was inhibited by HA, while the oxidation of Ara-C was enhanced by HA. Reaction of both 5-FU and Ara-C was influenced by water quality. Thus, this study provides new insights into the degradation of antineoplastic drugs.

Keywords: 5-Fluorouracil; Cytarabine; Potassium permanganate; Kinetics; Oxidative degradation

1. Introduction

Antineoplastic drugs have been widely used in cancer therapy, and the consumption continuously increased with the increasing incidence of cancer patient worldwide in recent decades [1–3]. In France, the consumption of antineoplastic drugs has exceeded 5,000 kg/year [1]. Most of the used antineoplastic drugs was excreted into hospital wastewater, and partly migrated to surface water as a result [4–8]. It has been reported that most of antineoplastic drugs and their metabolites are ecotoxic and genotoxic [9,10]. Therefore, particular attention should be paid to the removal of aquatic antineoplastic drugs.

Among these antineoplastic drugs, 5-fluorouracil (2,4-dioxo-5-fluoropyrimidine; 5-FU) and cytarabine (1-arabinofuranosylcytosine; Ara-C) are most commonly used [1]. 5-FU is often used for the therapy of colon, rectal, gastric and breast cancers, while Ara-C is mainly applied to cure acute leukemia. Although the majority of these compounds were metabolized in patient's body, 10%–20% was excreted in the parent form after 12–24 h [1]. 5-FU and Ara-C were detected up to several hundred $\mu g\cdot L^{-1}$ in hospital wastewater [11]. It has been reported that only 30% of 5-FU and

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47%–64% of Ara-C were removed in traditional biological wastewater treatment process [11,12]. The residual drugs in the effluent were released into the aquatic environment [1,13]. The median effective concentration (EC_{50}, reproduction toxicity to *Daphnia magna* growth inhibition) ranged from 5.2 to 45 $mg\cdot L^{-1}$ for 5-FU, and 63 to 810 $mg\cdot L^{-1}$ for Ara-C [9]. Therefore, it is necessary to develop efficient treatment method to remove 5-FU and Ara-C from hospital wastewater.

It has been reported that 5-FU was removed by UV, microorganisms, chlorine, bromine and ozone [14–18]. 5-FU was completely decomposed into intermediate products during those processes, while the removal efficiency of biodegradation was the slowest. The UV process can be enhanced by adding H_2O_2, Fe^{2+}/H_2O_2 and TiO_2. However, most of the intermediate products were resistant to further oxidation [15,17]. Ara-C was degraded in the gamma radiation and UV process [19–21]. H_2O_2, $K_2S_2O_8$ and TiO_2 enhanced the photocatalytic degradation of Ara-C. As an economical and efficient process, potassium permanganate ($KMnO_4$) has been widely used to remove organic pollutants over the past decades, and especially for the removal taste and odor in water and wastewater [22,23]. Jiang et al. [24] investigated the oxidation of phenolic endocrine disrupting chemicals (EDCs) by $KMnO_4$ in synthetic and real waters, and results showed that the second-order rate constant ($k_{Mn(VII)}$) of estrone, 17β-estradiol and estriol were 86.2, 81.9 and 87.4 $M^{-1}\cdot s^{-1}$, respectively, at pH 7.0. Hu et al. [25] investigated the oxidation of carbamazepine by $KMnO_4$ and obtained that the reaction kinetics followed a generalized second-order rate law, with apparent rate constant of 3.0×10^2 $M^{-1}\cdot s^{-1}$ at pH 7.0 and 25°C). However, the oxidative degradation of 5-FU and Ara-C in aqueous solution by $KMnO_4$ still has not been reported.

The purposes of this study were to: (1) determine the reaction kinetics of the 5-FU and Ara-C with $KMnO_4$ oxidation in aqueous solution and (2) investigate the effects of temperature, pH, humic acid (HA) and water quality on the oxidative degradation.

2. Materials and methods

2.1. Reagents

5-FU (purity > 99.0%) and Ara-C (purity > 98.0%) were obtained from Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan). The structural and chemical properties are listed in Table 1. Stock solutions of 5-FU (7.7 mM) and Ara-C (4.1 mM) were prepared with deionized water in amber flask separately and stored at 4°C for maximum 1 week prior to use. Both 5-FU and Ara-C were stable according to experimental results. Reaction solutions were obtained by appropriately diluting the stock solutions with deionized water. $KMnO_4$ (analytical reagent) was purchased from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). The stock solution of 0.2 M $KMnO_4$ was prepared with deionized water and stored in amber flask for no more than 30 d prior to use. Methanol and acetonitrile were both high performance liquid chromatography (HPLC) grade and purchased from Aladdin Industrial Corporation (Shanghai, China). All other reagents (ascorbic acid, sodium thiosulfate, acetic acid, sodium acetate, boric acid, sodium borate, sodium hydroxide, hydrochloric acid and phosphoric acid) were of analytical grade and purchased from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China).

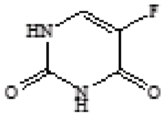
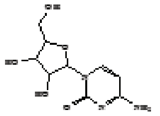
2.2. Experimental setup

2.2.1. Kinetics analysis

According to the results of pre-experiments, 5-FU reacts quickly with $KMnO_4$ because of the unsaturated C=C bonds in the central heterocyclic of 5-FU. Thus, low molar ratio of [5-FU]/[$KMnO_4$] was adopted in the experiment. The initial concentrations of 5-FU used in the kinetics experiment were 5, 7, 9 and 13 μM, and those of $KMnO_4$ were 20, 25, 35 and 40 μM. The reaction was performed in 250 mL beakers with 200 mL of working volume at 25.0°C ± 1.0°C. Solution pH was stable (pH = 7.0 ± 0.1) during whole reaction process; thus, no pH buffer was used. Reaction was started by adding $KMnO_4$ into target compound solution. One milliliter of reaction solution was periodically sampled, and 30 μL of ascorbic acid (20 mM) was added to the sample for quenching the reaction. No influence of acorbic acid on the degradation was observed according to control experiment. The sample was analyzed using HPLC after filtering through 0.45 μm glass fiber membrane.

As compared with 5-FU, the reaction rate of Ara-C was relatively slow when $KMnO_4$ was excess. Thus, the reaction were initiated by adding excess amount of $KMnO_4$ (200, 250, 300 and 400 μM) into Ara-C (5 μM) solution in which pH was controlled at 4.0 by acetate buffer (20 mM). The methods of sampling and separation processes were the same as described in the reaction of 5-FU.

Table 1
The structural and chemical properties of 5-FU and Ara-C

Target compound	Structure	Molecular formula	Molecular weight	pK_{a1}	pK_{a2}	UV_{max} (nm)
5-Fluorouracil (5-FU)		$C_4H_3FN_2O_2$	130.08	6.40	8.04	265
Cytarabine (Ara-C)		$C_9H_{13}N_3O_5$	243.22	4.22	Not available	271

2.2.2. Effect of environmental parameters

The effects of environmental parameters such as temperature, pH, HA and water quality on the reactions of 5-FU and Ara-C with $KMnO_4$ oxidation were investigated. The reaction was carried out in 250 mL beakers. The initial concentrations of 5-FU and $KMnO_4$ were set at 10 and 35 μM, respectively, while the concentrations of Ara-C and $KMnO_4$ were set at 5 and 300 μM, respectively.

For investigating the effect of temperature, reaction was conducted at temperature ranging from 5.0°C ± 1.0°C to 40.0°C ± 1.0°C. For investigating the effect of solution pH, acetate buffer (20 mM) was used to adjust solution pH from 3.0 to 5.8 under acidic conditions; the pH ranging from 7.4 to 10.0 was adjusted by borate buffer (20 mM) [24]. For investigating the effect of water quality, wastewater effluent and surface water were used. The wastewater treatment plant (WWTP) effluent was collected from Shiwuli WWTP, Hefei, China. The surface water was collected from Hubing Pond (surface water #1) and Dongpu Reservoir (surface water #2) in Hefei, China, respectively. The characteristics of the water and wastewater were summarized in Table 2.

2.3. Analysis

The concentrations of 5-FU and Ara-C were determined using an Agilent 1200 series HPLC with a diode array detector (DAD). The DAD detector was set at 265 and 271 nm for the detection of 5-FU and Ara-C, respectively. An Agilent HC-C18 (4.6 × 150 mm, 5 μm) column (USA) with an ECS C18 (4.6 × 10 mm, 5 μm) guard column (Elite, China) was used for the separation of target compounds. For the determination of 5-FU, the mixture of water (containing 0.1% formic acid) and acetonitrile (95/5, v/v) was used as mobile phase at a flow rate of 1.0 mL·min^{-1}. While for Ara-C, the mobile phase consisted of water (containing 0.4% phosphoric acid) and methanol (97/3, v/v).

All tests were conducted in triplicates, and the average values with the standard deviations were presented here.

3. Results and discussion

3.1. Kinetics analysis

3.1.1. Kinetics parameters of 5-FU

The reaction of 5-FU and $KMnO_4$ could be simply expressed as Eq. (1):

$$a[\text{5-FU}]_t + b[\text{KMnO}_4]_t \rightarrow \text{products} \quad (1)$$

where t represents reaction time; $[\text{5-FU}]_t$ represents the total concentration of 5-FU in aqueous solution at reaction time; $[\text{KMnO}_4]_t$ is the total concentration of $KMnO_4$ in aqueous solution at reaction time; and a and b are the coefficients of 5-FU and $KMnO_4$, respectively. Thus, the reaction rate can be expressed using Eq. (2):

$$-d[\text{5-FU}]/\text{dt} = k_{\text{app}}[\text{5-FU}]_t^{\,m}[\text{KMnO}_4]_t^{\,n} \quad (2)$$

where k_{app} is the apparent rate constant; m and n are the reaction orders of 5-FU and $KMnO_4$, respectively. The sum of m and n is the total kinetic order of the reaction. During the initial period of reaction time (within 1.0 min), the concentration of $KMnO_4$ was regarded as a constant. Eq. (2) can then be simplified to Eq. (3):

$$-d[\text{5-FU}]/\text{dt} = k_{\text{app}}'[\text{5-FU}]_t^{\,m} \quad (3)$$

where k_{app}' is the observed rate constant, which equals to $k_{\text{app}}[\text{5-FU}]_t^{\,m}$. Eq. (4) is obtained by evaluating the logarithm of the both sides of Eq. (3):

$$\ln\left(-d[\text{5-FU}]/\text{dt}\right) = \ln k_{\text{app}}' + m\ln[\text{5-FU}]_t \quad (4)$$

With the logarithm of initial reaction rate (ln[–d[5-FU]/dt]) as ordinate and the logarithm of the concentration of 5-FU ($\ln[\text{5-FU}]_t$) as abscissa, the value of m (the slope of the curve) was obtained. Similarly, the value of n can be obtained. Effects of different initial concentration of 5-FU and $KMnO_4$ were measured (Fig. 1). As shown in Fig. 2, the values of m and n were 0.77 and 0.86, respectively. Thus, the total kinetic order of the reaction was 1.63. Therefore, the reaction rate was described using Eq. (5):

$$-d[\text{5-FU}]/\text{dt} = k_{\text{app}}[\text{5-FU}]_t^{\,0.77}[\text{KMnO}_4]_t^{\,0.86} \quad (5)$$

The total reaction order (the sum of m and n) was not an integer, which indicated that the reaction may contain multiple elementary steps [7]. The reaction order was found to be 0.77 in terms of 5-FU and 0.86 in terms of $KMnO_4$, which implied that the concentration change of $KMnO_4$ might be slightly more effective to the reaction rate than 5-FU. When doubling the concentration of $KMnO_4$, an 80% increase of the reaction rate was observed; while doubling the concentration of 5-FU, the corresponding value was 70%.

All parameters of the batch experiments were listed in Table 3. Based on these parameters and the derived equations,

Table 2
Characteristics of the water and wastewater

Waters	pH	TOC (mg·L^{-1})	COD (mg·L^{-1})	NH_4^+–N (mg·L^{-1})	PO_4^{3-} (mg·L^{-1})	NO_3^-–N (mg·L^{-1})	NO_2^-–N (mg·L^{-1})
WWTP effluent	7.11	5.78	25	2.78	1.25	13.1	0.91
Surface water #1	7.21	8.27	35	1.68	0.065	0.36	0.66
Surface water #2	7.05	0.76	14	0.22	0.20	0.10	0.09

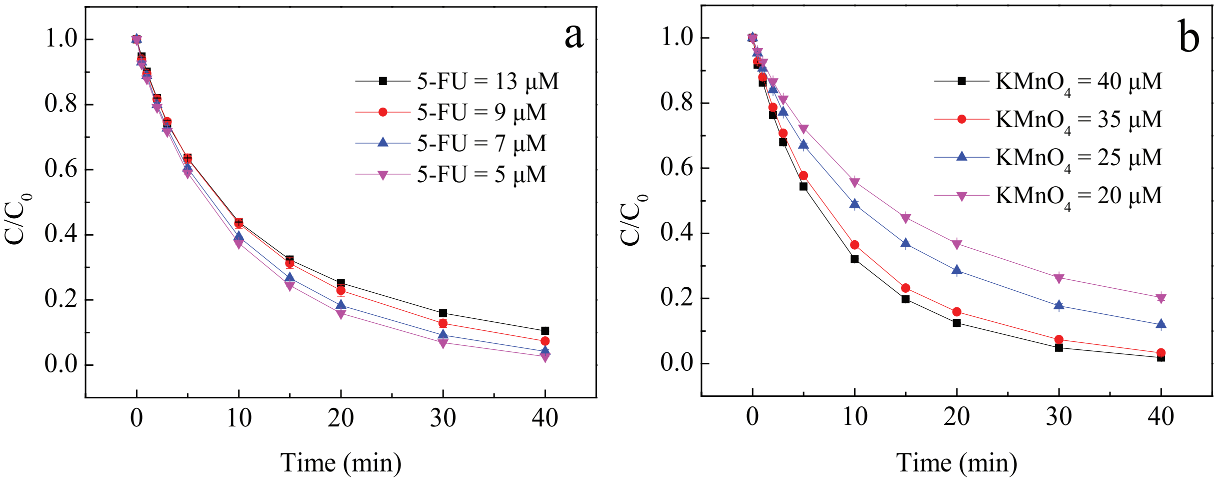


Fig. 1. Effect of different initial concentration of (a) 5-FU ([5-FU] = 5–13 μM, [$KMnO_4$] = 30 μM) and (b) $KMnO_4$ ([5-FU] = 5 μM, [$KMnO_4$] = 20–40 μM) at 25°C.

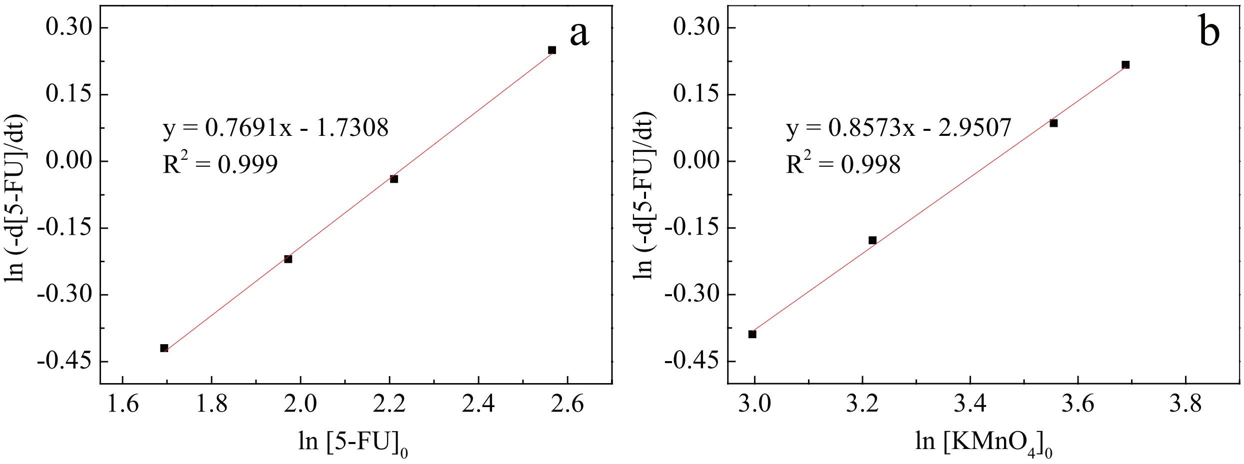


Fig. 2. The relationship between the initial reaction rate and the concentration of (a) 5-FU ([5-FU] = 5–13 μM, [$KMnO_4$] = 30 μM) and (b) $KMnO_4$ ([5-FU] = 5 μM, [$KMnO_4$] = 20–40 μM) at 25°C.

Table 3
Reaction conditions and k_{app} of all batch experiments of 5-FU

$[5\text{-FU}]_0$ (μM)	$[KMnO_4]_0$ (μM)	$-d[5\text{-FU}]/dt$ (μM·min^{-1})	k_{app} ($\times10^{-4}$ μM$^{-0.63}$·s^{-1})
13.01	30	1.29	1.60
9.12	30	0.96	1.57
7.19	30	0.80	1.57
5.44	30	0.66	1.60
9.06	40	1.24	1.58
9.00	35	1.09	1.57
8.97	25	0.84	1.62
9.18	20	0.68	1.57
		Average	1.58

k_{app} values under different conditions were calculated. The mean k_{app} value of 1.58 × 10^{-4} μmol$^{-0.63}$·s^{-1} was obtained. Thus, the kinetics equation of the 5-FU was developed, as shown in Eq. (6):

$$-d[5\text{-FU}]/\mathrm{d}t = 1.58\times10^{-4}\times[5\text{-FU}]_t^{0.77}[KMnO_4]_t^{0.86} \tag{6}$$

3.1.2. Kinetics parameters of Ara-C

When the amount of $KMnO_4$ was excess, the concentration of $KMnO_4$ can be regarded as a constant. The reaction of Ara-C (5 μM) with $KMnO_4$ oxidation followed the pseudo-first-order rate law (as shown in Fig. 3). All measured pseudo-first-order rate constants (k_{obs}, min^{-1}) were listed in Table 4. The reaction rate of this reaction can be expressed by Eq. (7):

$$-d[Ara-C]/\mathrm{d}t = k_{obs}[Ara-C]_t \tag{7}$$

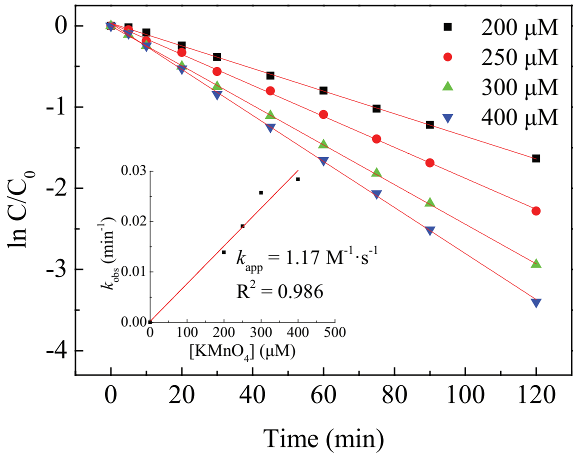


Fig. 3. Oxidation of Ara-C when the concentration of $KMnO_4$ was in excess at 25°C ([Ara-C] = 5 μM, [$KMnO_4$] = 200–400 μM, pH 4.0).

Table 4
The reaction conditions and fitting relative deviation of Ara-C

[Ara-C] (μM)	[$KMnO_4$] (μM)	k_{obs} (min^{-1})	R^2
5	200	0.0139	0.999
5	250	0.0191	0.999
5	300	0.0244	0.999
5	400	0.0284	0.999

where t represents reaction time; [Ara-C]$_t$ represents the total concentration of Ara-C in aqueous solution at reaction time; and k_{obs} is the pseudo-first-order rate constant.

The inset in Fig. 3 confirmed that the k_{obs} measured at various concentrations of $KMnO_4$ at pH 4.0 were linear with $KMnO_4$ concentration, which demonstrated that the reaction also be first order with respect to $KMnO_4$. Thus, the oxidation of Ara-C by $KMnO_4$ followed a generalized second-order rate law. The value of k_{app} (the slope of the inset figure in Fig. 3) was 1.17 $M^{-1}\cdot s^{-1}$ at pH 4.0 and 25°C. Thus, the kinetics equation of the Ara-C was obtained, as shown in Eq. (8). It has been reported that the reaction k_{app} of ciprofloxacin, trimethoprim and lincomycin with $KMnO_4$ were 0.61, 1.6 and 3.6 $M^{-1}\cdot s^{-1}$, respectively (pH 7.0, 25°C) [26]. This result indicated that the reaction rate of Ara-C with $KMnO_4$ was much slower than that of trimethoprim and lincomycin, but faster than ciprofloxacin. And the Ara-C was easily decomposed by UV, UV/H_2O_2 and UV/$K_2S_2O_8$ than $KMnO_4$ according to previous results [19].

$$-d[\text{Ara-C}]/\text{dt} = 1.17 \times [\text{Ara-C}]_t[\text{KMnO}_4]_t \quad (8)$$

3.2. Effect of temperature

The oxidation of 5-FU and Ara-C by $KMnO_4$ exhibited great temperature dependence. With the increase of temperature from 5°C to 40°C, the degradation rates of the two target compounds increased significantly (as shown in Fig. 4). As shown in Fig. 5, there was a linear relationship between k_{app} and the reciprocal of absolute temperature (T). Arrhenius equation was used to determine the apparent activation energy (E_a), as shown in Eq. (9) [25]:

$$\ln k_{app} = \frac{-E_a}{R} \cdot \frac{1}{T} + \ln A \quad (9)$$

where E_a is the apparent activation energy (kJ·mol^{-1}); R is the universal gas constant (J·mol^{-1}·K); T is absolute temperature (K); and A is the Arrhenius pre-exponential constant. By fitting measured experimental data to Arrhenius equation, the E_a of 5-FU and Ara-C were 32 and 40 kJ·mol^{-1}, respectively, which indicated that 5-FU could be easily oxidized by $KMnO_4$ than Ara-C. Hu et al. [25] reported that the E_a of carbamazepine by $KMnO_4$ was 22 kJ·mol^{-1}. The lower E_a of carbamazepine indicated that 5-FU and Ara-C were more difficult to be decomposed by $KMnO_4$ than carbamazepine.

3.3. Effect of pH

The reaction kinetics of 5-FU and Ara-C with $KMnO_4$ were obviously dependent on pH. As shown in Fig. 6, the k_{app} of 5-FU increased from 0.76×10^{-4} $\mu M^{-0.63}\cdot s^{-1}$ to 1.73×10^{-4} $\mu M^{-0.63}\cdot s^{-1}$ when the pH increased from 3.0 to 9.0. Under acid and alkaline conditions, two k_{app} peak values of 1.72×10^{-4} $\mu M^{-0.63}\cdot s^{-1}$ at pH 4.0 and 1.73×10^{-4} $\mu M^{-0.63}\cdot s^{-1}$ at pH 7.4 were obtained, respectively. The pK_{a1} and pK_{a2} of 5-FU were 6.40 and 8.04, respectively [16], which indicated that there was ionized 5-FU at pH 7.4 solution. Such species were easily oxidized that resulted in the maximum k_{app} of 5-FU at pH 7.4. In addition, the oxidative activity of $KMnO_4$ was great in acidic conditions, so 5-FU was also relatively easy to be degraded by $KMnO_4$. For example, the reaction of trimethoprim was rapid under acidic conditions [26].

However, the pH had different influence on the oxidation kinetics of Ara-C. The reaction rate was slow under weak acid and alkaline conditions, as shown in Fig. 6. While as the pH decrease from 9.0 to 3.5, the value of k_{app} increased obviously. The highest k_{app} 1.52 $M^{-1}\cdot s^{-1}$ was obtained at pH 3.5. Because the pK_{a1} of Ara-C was 4.22, Ara-C was mainly in the form of non-ionization at pH 3.5. But the pK_a of $KMnO_4$ was –2.25 [25]; the $HMnO_4$ must exist in the reaction solution that may lead to the enhancement of the Ara-C reaction at pH 3.5. Further research will be needed to elucidate the reason of the pH influence on 5-FU and Ara-C reactions.

3.4. Effect of HA

As one kind typical dissolved organic matter, the humic substances are commonly exist in surface waters with concentration from 0 to 30 mg·L^{-1}. It has been reported that the presence of the HA in water had influence on the chemical oxidation process of micro drugs [27–29]. Therefore, HA was added to the reaction solutions, and the oxidative degradation of 5-FU was inhibited by HA, while the oxidation of Ara-C was enhanced by HA.

For the oxidation of 5-FU, the reaction was inhibited by HA, and the degree of inhibition increased with the increase of HA (Fig. 7(a)). This result was caused by the

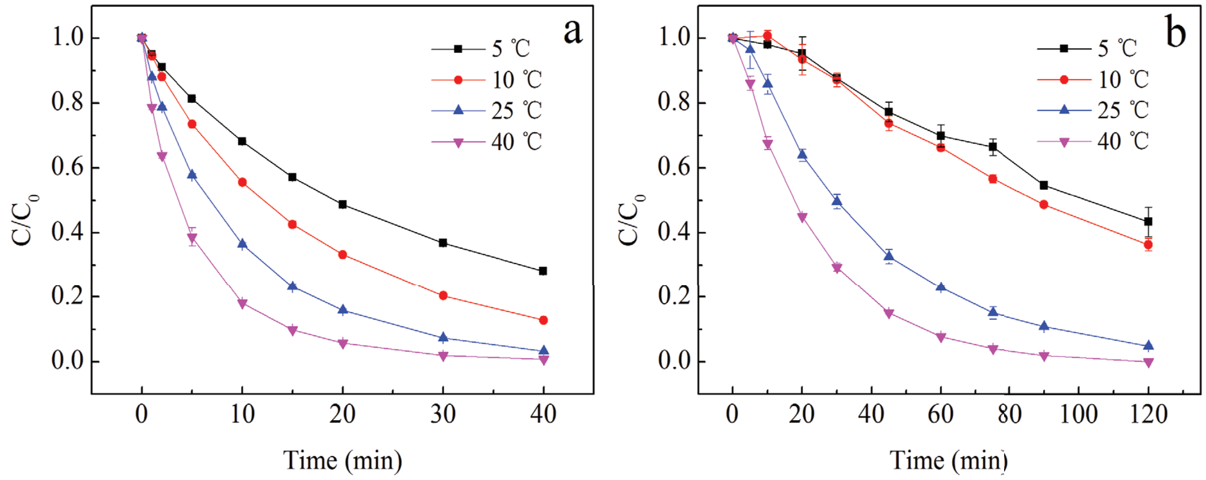


Fig. 4. Effect of temperature on the reaction rate of (a) 5-FU ([5-FU] = 10 μM, [$KMnO_4$] = 35 μM) and (b) Ara-C ([Ara-C] = 5 μM, [$KMnO_4$] = 300 μM, pH 4.0).

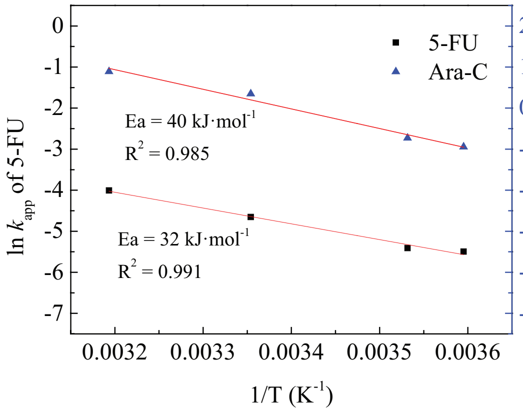


Fig. 5. The relationship between temperature and the k_{app} of 5-FU ([5-FU] = 10 μM, [$KMnO_4$] = 35 μM) and Ara-C ([Ara-C] = 5 μM, [$KMnO_4$] = 300 μM, pH 4.0).

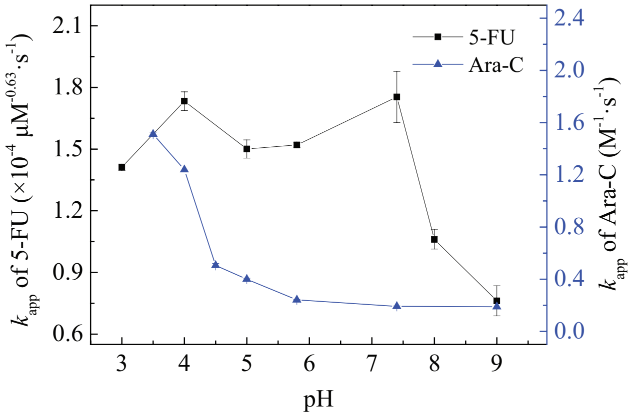


Fig. 6. Effect of pH on the oxidation of 5-FU ([5-FU] = 10 μM, [$KMnO_4$] = 35 μM) and Ara-C ([Ara-C] = 5 μM, [$KMnO_4$] = 300 μM) at 25°C.

competitive effect between HA and target compound 5-FU, which was similar to the effect of dissolved organic matters [30].

In contrast, the oxidation of Ara-C was enhanced with the increase of HA concentration in the solution (Fig. 7(b)). According to recent studies, there were also enhancement caused by HA in the oxidation of bisphenol A by permanganate [31,32]. In the whole reaction process, there was inevitably producing manganese dioxide, which was often acted as catalyst. Further studies confirmed that the HA can accelerate the formation of manganese dioxide [27,32]. Thus, the observed enhancement in this experiment may be caused by the catalyst manganese dioxide. Meanwhile, other studies indicated that the oxidation of phenols by permanganate was correlated well with the aromaticity and specific visible absorption (SVA) at 665 nm of HA [33].

3.5. Effect of water quality

Water and wastewater were collected to investigate the effect of water quality on the reaction rates in this study. As observed in Fig. 8, in all three testing conditions, reaction rates of both 5-FU and Ara-C were the fastest in the deionized water. Due to more dissolved organic matters contained in the surface water #1, the reaction rate of 5-FU was lowest in this situation (Fig. 8(a)). Similarly, the richest organic matters contained in WWTP effluent also caused the lowest oxidation rates of Ara-C (Fig. 8(b)). It is important to note that the influences of the WWTP effluent on these two reactions were different. The WWTP effluent had greater negative effect on the reaction of 5-FU. The removal rate of 5-FU was decreased by 40%; while for Ara-C, the corresponding value was only 10%. In the reactions of 5-FU and Ara-C, the concentrations of $KMnO_4$ were 35 and 300 μM, respectively. Thus, it was speculated that a larger proportion of $KMnO_4$ was consumed by

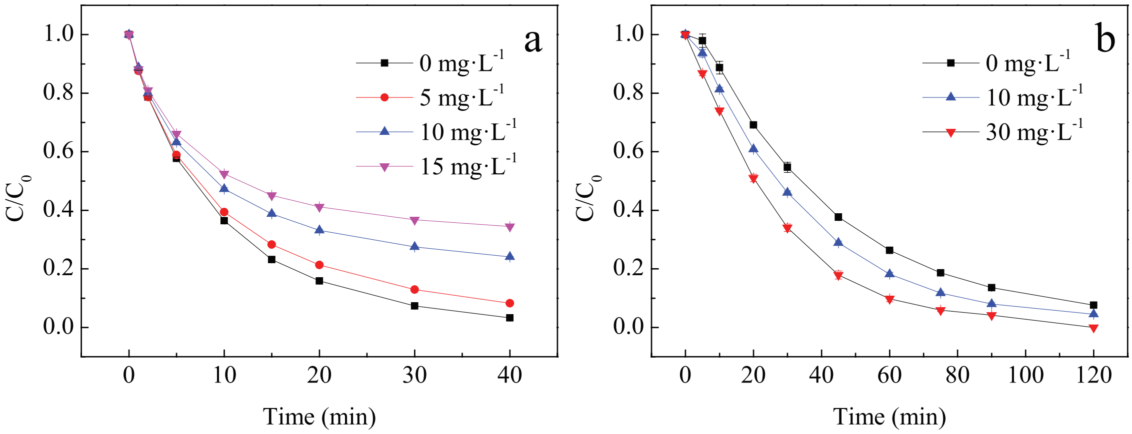


Fig. 7. Effect of HA on the oxidation of (a) 5-FU ([5-FU] = 10 μM, [$KMnO_4$] = 35 μM) and (b) Ara-C ([Ara-C] = 5 μM, [$KMnO_4$] = 300 μM, pH 4.0) at 25°C.

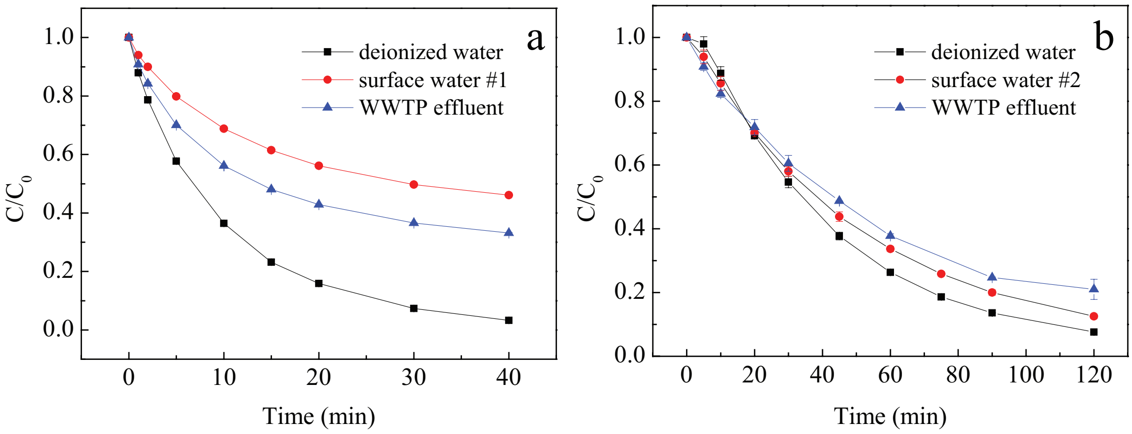


Fig. 8. Effect of water quality on the oxidation of (a) 5-FU ([5-FU] = 10 μM, [$KMnO_4$] = 35 μM) and (b) Ara-C ([Ara-C] = 5 μM, [$KMnO_4$] = 300 μM, pH 4.0) at 25°C.

organic matters during the degradation process of 5-FU as compared with Ara-C, which means the organic matters had greater influence on the reaction of 5-FU.

4. Conclusion

Antineoplastic drugs 5-FU and Ara-C were degraded effectively by $KMnO_4$ oxidation in aqueous solution. According to the dynamic experiments, the kinetics model of 5-FU was $-d[\text{5-FU}]/dt = k_{app}[\text{5-FU}]_t^{0.77}[\text{Mn(VII)}]_t^{0.86}$. The reaction kinetics of Ara-C followed a generalized second-order rate law. All k_{app} values were dependent on temperature, pH, water quality and HA. Because the E_a of 5-FU and Ara-C were 32 and 40 kJ·mol^{-1}, respectively, it can be deduced that the 5-FU may be slightly easily decomposed than Ara-C by $KMnO_4$. The maximum k_{app} value of 5-FU was 1.73×10^{-4} μM$^{-0.63}$·s^{-1} at pH 7.4, while Ara-C was 1.52 M^{-1}·s^{-1} at pH 3.5. The water quality had significant influence on the reaction of 5-FU and Ara-C. The degradation of 5-FU was inhibited by the HA, while the oxidation of Ara-C was enhanced.

Acknowledgments

This research was partly supported by the National Natural Science Foundation of China (51578205, 51108149), the Fundamental Research Funds for the Central Universities (JZ2016HGTB0722) and the Open Topic of State Key Laboratory of Pollution Control and Resource Reuse (PCRRF11014).

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