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Oxidative transformation of antiretroviral drug zidovudine during water treatment with permanganate: reaction kinetics and pathways

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ABSTRACT

The presence of the pharmaceutical substances in the water has been reported by many studies and has attracted attention across the world. The mechanistic insight into oxidation of antiretroviral drug zidovudine (ZDV) by potassium permanganate was investigated between the pH values 3.0 and 9.0. The pH-dependent second-order rate constants were determined and rate constants decreased with an increase in pH. The products of the reaction were identified by high-resolution mass spectrometry. A probable mechanism is proposed which involves the formation of an intermediate complex between permanganate and ZDV, which further undergoes degradation in subsequent fast steps to form various oxidized products. The different parameters like effect of initially added products, solvent polarity, ionic strength, temperature, and pH on the rate of the oxidative degradation of ZDV by permanganate were systematically studied. The various activation parameters were determined from the effect of variation in temperature on the oxidative degradation of ZDV by permanganate in acidic medium and discussed in detail.

Keywords: Degradation; Zidovudine; Permanganate; Kinetics; Mechanism

1. Introduction

The consumption of the pharmaceutical compounds has been rapidly increasing due to the huge population growth across the world [1]. As a result of this, there has been a rapid development in the pharmaceutical industries across the world [2]. Pharmaceutical compounds (PhACs) enter into environment through numerous ways. It is predicted that 25–33% of PhACs are not disposed properly and turn up in a landfill or wastewater treatment plant [3]. Waste streams from industrial manufacturing that contain PhACs are discharged to water resources through regulated and unregulated practices.

Due to the rapid increase in the population and limited number of sources of potable water, it is now very essential for us to check that drinking water will be safe, accessible, and plentiful for everyone in the days to come. There are many oxidation techniques have been projected to reduce the toxic contaminants in water [4,5].

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Potassium permanganate finds widespread uses in organic synthesis as an oxidant [6,7]. In both media, acidic [8] and alkaline [9–11], permanganate is the most competent and powerful oxidizing agent. Permanganate is reduced to manganese dioxide and precipitates out of the solution [12]. Permanganate reduces to MnO_2 in a neutral medium.

$$2H_2O + MnO_4^- + 3e^- \rightarrow MnO_2 + 4OH^- \tag{1}$$

Permanganate is the most ideal oxidant as compared to other available oxidants due to its reasonably low cost, ease of using, better stability, and efficacy for a broad pH range [13]. Oxidative degradation of organic matter by permanganate does not direct to the formation of any harmful halogenated (brominated or chlorinated) side products but it leads to the formation of innocuous side products [14]. Permanganate being a green oxidizing agent has spread significant awareness [15] and extensively used both in drinking water treatment for eliminating microcontaminants and enhancing coagulation [16] as well as remediation of polluted groundwater [17,18]. Intermediates of manganese have long lifetimes and an oxidation state of these intermediates provides useful conclusions for the plausible mechanisms of reactions involving the nature of the intermediates.

Zidovudine (ZDV) (3´-Azido-3´-deoxythymidine) is also called as azidothymidine (AZT). This is a type of antiretroviral drug prescribed for the treatment of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) infection. ZDV is found to be effective against HIV *in vivo*, which has led to its chronic use in patients with AIDS [19]. The value of dissociation constant pK_a for ZDV is 9.68 [20]. The solubility of ZDV in water is 25 mg mL^{-1} at 25˚C [21]. The structure of the ZDV is shown in Fig. 1.

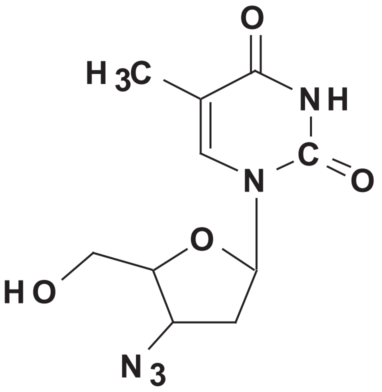

Fig. 1. Structure of the ZDV.

As per the extensive literature survey carried out for the permanganate redox reactions, it is found that there are no reports on the investigation of oxidative degradation of ZDV by permanganate in acidic medium. Investigation of the oxidative degradation of ZDV by permanganate in acidic medium is significantly important to understand the mechanistic profile of ZDV in oxidation–reduction reaction and to arrive at a suitable mechanism for the oxidation of ZDV by permanganate based on the kinetic outcome.

2. Experimental

2.1. Chemical reagents

A suitable amount of ZDV sample compound was dissolved in double-distilled water in order to prepare a stock solution of ZDV. Potassium permanganate of analytical grade was obtained from MERCK Specialties Pvt. Ltd and used without further purification. As per the standard procedure laid down, a suitable concentration of potassium permanganate stock solution was prepared by dissolving a predetermined amount of potassium permanganate crystals in double-distilled water [22]. During the kinetic experimental studies, 0.02 mol dm^{-3} acetate buffer (pH 3–5), phosphate buffer (pH 6.0–7.0), and borate buffer (pH 8.0–9.0) were mixed in the reaction mixture for keeping the pH constant. During the kinetic experiment of the oxidative degradation of ZDV by permanganate, freshly prepared solutions were used.

2.2. Instruments used for the kinetic studies and product analysis

(a) For the kinetic studies of the reaction mixture, A CARY 50 Bio UV–vis Spectrophotometer (Varian BV, The Netherlands) with temperature controller was used.
(b) For the product analysis of the reaction mixture of the oxidative degradation of ZDV by permanganate in acidic medium, high-performance liquid chromatography (HPLC) system (Shimadzu prominence) and high-resolution mass spectrophotometer (HR-MS) system (Thermo Scientific Q Exactive) along with a column Thermo Scientific Hypersil Gold C18 having dimension 150 × 4.6 mm–8 μm were used.
(c) In order to measure the required pH of a reaction mixture, Elico pH meter (Model Li 120) was used during an experiment.

2.3. Kinetic procedure

Pseudo-first-order conditions were potted to study the kinetics of the oxidative degradation of ZDV by permanganate, where the concentration of ZDV was maintained 10 times more as compared to the concentration of permanganate at temperature 25 ± 0.2˚C. Freshly prepared solutions of ZDV, buffer, and potassium permanganate were placed in the thermostat independently in order to achieve the uniform temperature. These reagents are then mixed using their requisite concentration to start the oxidative degradation of ZDV by permanganate.

Using UV–vis spectrophotometer, the decrease in the concentration of permanganate oxidant during the redox reaction was monitored at λ_{max} 526 nm with respect to time. Verification of Beer's law was performed by varying the concentrations of permanganate at the wavelength 526 nm. This verification gives molar absorptivity 2,283 ± 20 dm^3 mol^{-1} cm^{-1} which is close to the literature value 2,200 dm^3 mol^{-1} cm^{-1}. There is no significant interference from other species of the reaction mixture at 526 nm [23]. The values of the pseudo-first-order rate constants were determined by plotting the graph of log (absorbance) vs. time as shown in the Fig. 2. The straight line graphs were obtained for different concentrations of permanganate which shows that the order is unity with respect to permanganate. The spectral changes of the oxidation of ZDV by permanganate using spectrophotometer were shown in Fig. 3. The two isosbestic points as observed in this figure show that the interconversion of heptavalent manganese to both blue (Mn^{5+}) and green (Mn^{6+}) species at around the absorption maxima of 475 and 575 nm.

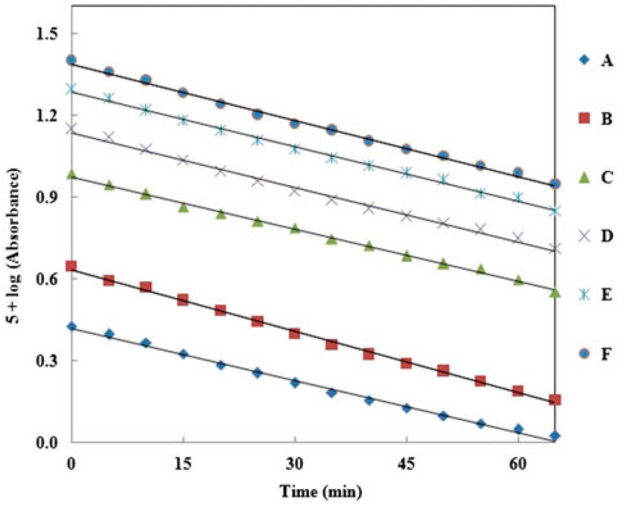

Fig. 2. Pseudo-first-order plots of the oxidative degradation of ZDV by permanganate in acidic medium at 298 K. [MnO$_4^-$] × 10^4 mol dm^{-3} (A) 0.25, (B) 0.50, (C) 1.0 (D), 1.5, (E) 2.0, (F) 2.5. [ZDV] = 1 × 10^{-3} mol dm^{-3}, [buffer] = 6 × 10^{-3} mol dm^{-3}, ionic strength (I) = 0.02 mol dm^{-3}.

HPLC system with "190 PDA" (photo diode array) detector (Shimadzu prominence) was used for the product analysis. The reaction mixture was filtered using spin-pure disposable syringe filters. The mobile phase used for the analysis was a mixture of acetonitrile and water in the ratio of 50:50. The Thermo Scientific Q Exactive HR-MS was used to identify the degraded products of the oxidative degradation of ZDV by permanganate. The column Thermo Scientific Hypersil Gold C18 having dimension 150 × 4.6 mm–8 μm was used for the analysis.

2.4. Product identification method

In order to initiate the oxidative degradation reaction of the ZDV by permanganate, a suitable amount of ZDV was added with phosphate buffer of pH 6. Higher concentration of permanganate solution was used to degrade the antiretroviral drug ZDV. In order to accomplish the reaction, the reaction mixture was placed for a period of 20 h to form degraded products. Then, this reaction mixture was used for the identification of various oxidation products of ZDV. A suitable amount of the reaction mixture was used for the HR-MS analysis. The flow rate 500 μL/min was kept for the analysis. The pressure 33.2 bar was maintained. The ratio 50:50 of acetonitrile and water mixture was used as mobile phase. Hypersil Gold C18 column was used for the analysis. The sample analysis was carried out using positive mode electrospray ionization (ESI$^+$)

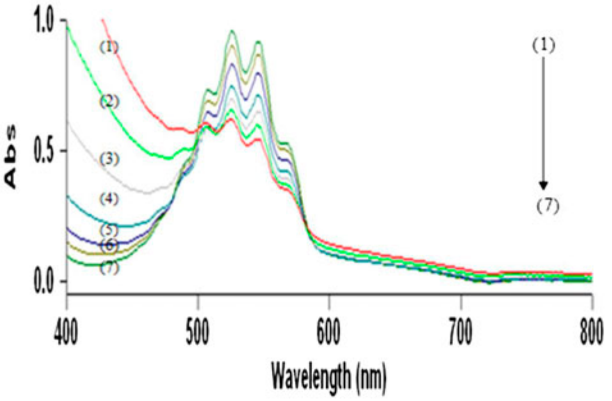

Fig. 3. UV–visible spectral changes occurring in the oxidative degradation of the ZDV by permanganate in the acidic medium. Time: (1) 0.00 min, (2) 0.50 min, (3) 1.00 min, (4) 1.50 min, (5) 2.00 min, (6) 2.50 min, and (7) 3.00 min.

over a mass scan range varies from 100 to 800 m/z. The data collected from the HR-MS were used to identify the different degradation products and are listed in the Table 1. The molecular ion peaks of these degraded products are shown in Fig. 4.

3. Results

3.1. Reaction orders

The oxidative degradation of ZDV by permanganate in acidic condition proceeds with a measurable rate. Experimental orders with respect to ZDV, permanganate, and H^+ have been determined from the slope of log k vs. log (concentration) for the oxidative degradation of ZDV by permanganate in acidic condition. From these plots, the rate of the reaction for the oxidative degradation of ZDV by permanganate in terms of orders of ZDV, permanganate, and H^+ by applying rate law can be written as follows:

$$\text{Rate} = \frac{-\mathrm{d}[\mathrm{MnO}_4^-]}{\mathrm{d}t} = \mathrm{k}\,\mathrm{K}_1\,\mathrm{K}_2\left[\mathrm{MnO}_4^-\right][\mathrm{ZDV}][\mathrm{H}^+] \qquad (2)$$

3.2. Effect of concentration of permanganate on the rate of the reaction

The effect of variation in concentration of permanganate on the oxidative degradation of ZDV by permanganate in acidic medium was studied by varying the concentration of permanganate from the range of 2.5×10^{-5} to 2.5×10^{-4} mol dm^{-3} while keeping other conditions constant i.e. concentration of ZDV = 1×10^{-3} mol dm^{-3} and concentration of buffer = 0.02 mol dm^{-3} in order to maintain pH and constant ionic strength. Plots of log (absorbance) vs. time for different concentration of permanganate were found in straight lines which indicate that experimental order with respect to permanganate is unity.

3.3. Effect of concentration of ZDV on the rate of the reaction

To study the effect of ZDV on the rate constant for the oxidative degradation of ZDV by permanganate in acidic medium, concentration of ZDV was varied from the range of 5×10^{-4} to 3.0×10^{-3} mol dm^{-3} while keeping other conditions constant i.e. concentration of permanganate = 1×10^{-4} mol dm^{-3}, and concentration of buffer = 0.02 mol dm^{-3} in order to maintain pH and constant ionic strength at temperature 25 ± 0.2˚C. From the kinetic experiment, it is observed that the rate constant (k_{obs}) increases with increase in the concentration of ZDV for oxidative degradation of ZDV by permanganate in acidic medium as shown in Fig. 5. After plotting the graphs of log k_{obs} vs. log [ZDV] for the oxidative degradation of ZDV by permanganate in acidic medium, it is observed that the

Table 1
Identified degraded products of ZDV during oxidation with permanganate by HR/MS analysis

ZDV products	$t_{R(Min)}$[a]	$M + H^+$/ $M + Na^+$ measured	Theoretical mass (Da)	Molecular formula	Difference in measured and theoretical mass	Name of the identified compounds
ZDV_P11	2.14	181.96	181.10	$C_5H_6N_2O_4$	+0.86	3-Hydroxy-5-hydroxymethyl-1H-pyrimidine-2,4-dione
ZDV_P21	3.42	224.07	224.21	$C_{10}H_{12}N_2O_4$	−0.14	1-(5-Hydroxymethyl-2,5-dihydro-furan-2-yl)-5-methyl-1H-pyrimidine-2,4-dione
ZDV_P22	3.42	239.91	238.20	$C_{10}H_{10}N_2O_5$	+1.71	5-(5-Methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2,5-dihydro-furan-2-carboxylic acid
ZDV_P31	3.42	149.02	126.11	$C_5H_6N_2O_2$	−0.08	5-Methyl-1H-pyrimidine-2,4-dione
ZDV_P32	2.14	113.09	113.11	$C_5H_7NO_2$	−0.02	N-(2-Methyl-3-oxo-propenyl)-formamide
ZDV_P41	2.14	140.90	141.13	$C_5H_7N_3O_2$	−0.23	(3-Azido-2,3-dihydro-furan-2-yl)-methanol
ZDV_P42	2.14	114.05	115.13	$C_5H_9NO_2$	−1.08	(3-Amino-2,3-dihydro-furan-2-yl)-methanol
ZDV_P43	2.14	130.90	131.13	$C_5H_9NO_3$	−0.23	(3-Hydroxyamino-2,3-dihydro-furan-2-yl)-methanol

[a] $t_{R(Min)}$ indicates retention time in minutes.

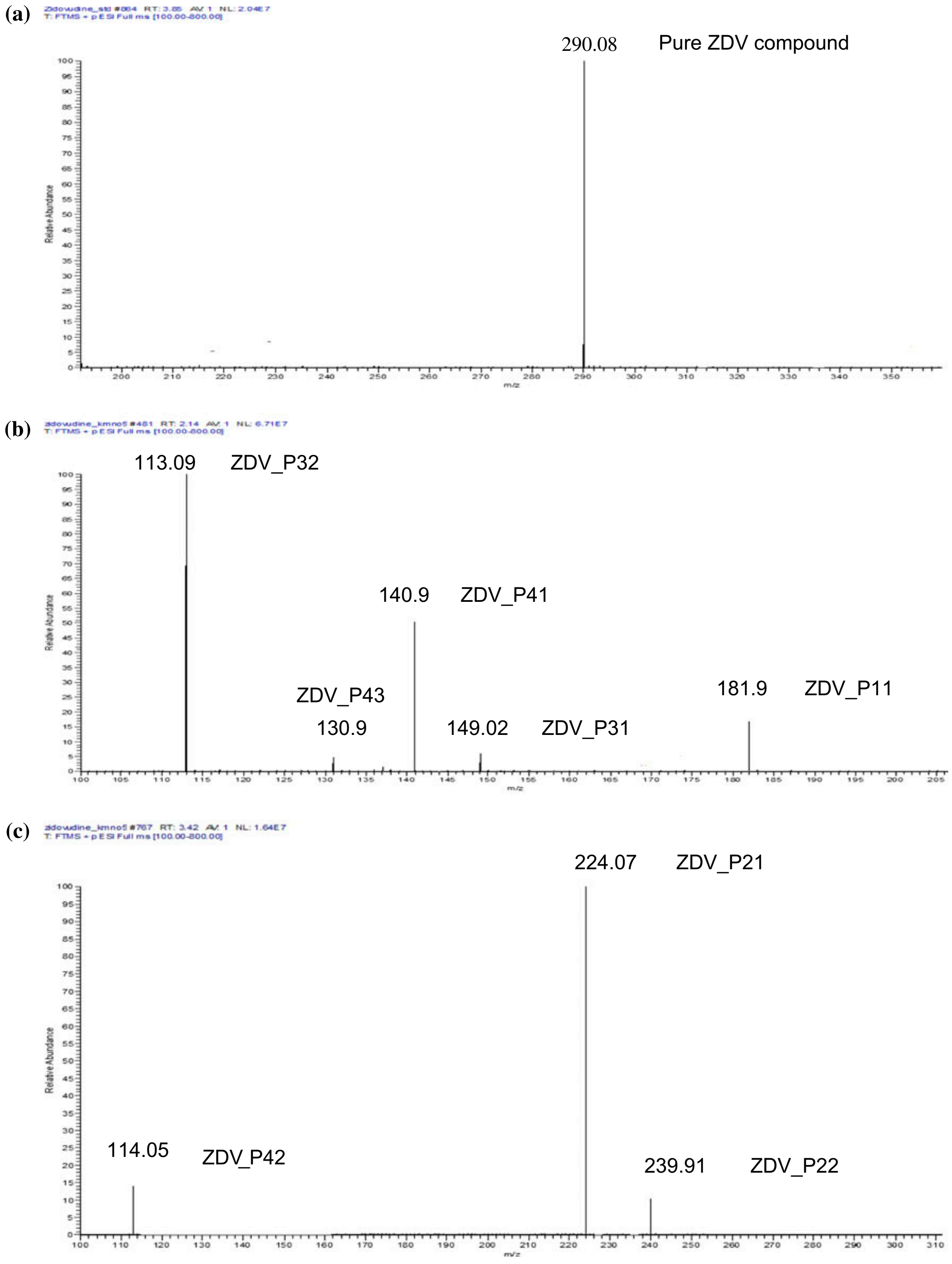

Fig. 4. HR-MS spectra of: (a) pure ZDV with its molecular ion peak m/z at 290.08, (b) oxidation products of ZDV by permanganate with its molecular ion peaks m/z at 113.09 for ZDV-P32, 130.9 for ZDV_P43, 140.9 for ZDV_P41, 149.02 for ZDV_P31, and 181.9 for ZDV_P11, and (c) oxidation product of ZDV by permanganate with its molecular ion peaks m/z at 114.05 for ZDV_P42, 224.07 for ZDV_P21, 239.91 for ZDV_P22.

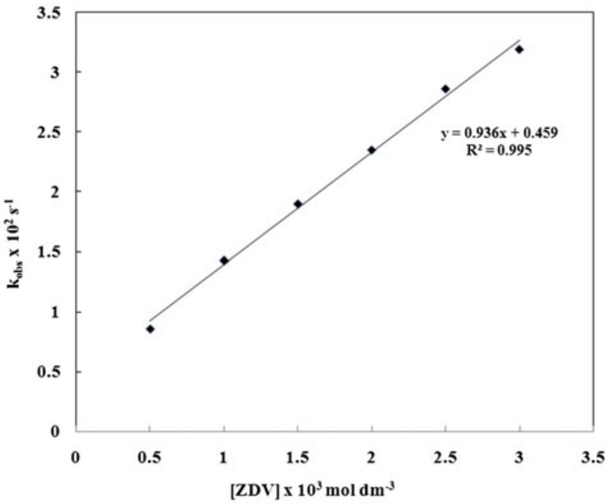

Fig. 5. Effect of variation in concentration of ZDV on the oxidative degradation of ZDV by permanganate at 298 K. [ZDV] = 5×10^{-4} to 3×10^{-3} mol dm^{-3}, [MnO_4^-] = 1×10^{-4} mol dm^{-3}, [buffer] = 6×10^{-3} mol dm^{-3}, ionic strength (I) = 0.02 mol dm^{-3}.

order with respect to ZDV is less than unity (0.73) ($R^2 > 0.999$).

3.4. Effect of ionic strength on the rate of the reaction

By keeping concentration of permanganate = 1×10^{-4} mol dm^{-3} and concentration of ZDV = 1×10^{-3} mol dm^{-3} constant for the oxidative degradation of ZDV by permanganate in acidic medium, the concentration of buffer having pH 6 was varied from the range of 0.002–0.012 mol dm^{-3}. It is observed from the experimental data of kinetics that variation in ionic strength (I) does not have any considerable effect on the values of the rate constant for the oxidative degradation of ZDV by permanganate in acidic medium.

3.5. Effect of solvent polarity on the rate of the reaction

To study the effect of solvent polarity on the oxidative degradation of ZDV by permanganate in acidic medium, the volume of tertiary butanol was varied by keeping other conditions constant i.e. concentration of permanganate = 1×10^{-4} mol dm^{-3}, concentration of ZDV = 1×10^{-3} mol dm^{-3}, and concentration of buffer = 0.02 mol dm^{-3}. The data obtained from kinetics show that as the volume of tertiary butanol increases, the values of rate constant decrease. It indicates that as the solvent polarity decreases due to increase in the volume of tertiary butanol, the rate of the reaction decreases. The plot of log k_{obs} vs. $1/D$ was linear with positive slope as shown in the Fig. 6.

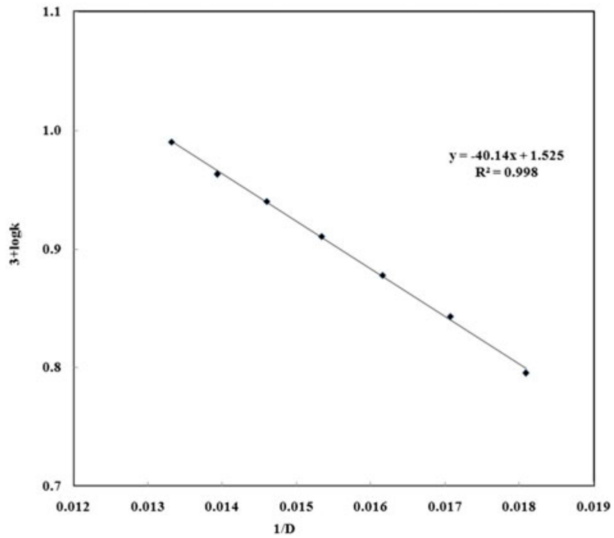

Fig. 6. Effect of solvent polarity on oxidative degradation of ZDV by permanganate in acidic medium at 298 K by varying the concentration of t-butanol. [MnO_4^-] = 1×10^{-4} mol dm^{-3}, [ZDV] = 1×10^{-3} mol dm^{-3}, [buffer] = 6×10^{-3} mol dm^{-3}, ionic strength (I) = 0.02 mol dm^{-3}.

3.6. Effect of the initially added product on the rate of the reaction

MnO_2 was added initially into the reaction mixture of ZDV and permanganate in acidic condition. After adding MnO_2, there was no considerable change observed in the rate constant of the oxidative degradation of ZDV by permanganate reaction in the acidic medium.

3.7. Polymerization study for the involvement of free radical

A suitable amount of acrylonitrile monomer was added into the reaction mixture for the oxidative degradation of ZDV by permanganate in acidic condition. This mixture was kept in an inert atmosphere for the period of 7 h. Then, the reaction mixture was diluted with the help of methyl alcohol. During the dilution by methyl alcohol, there was no formation of an insoluble precipitate. This polymerization study reveals that there is no involvement of any free radical in oxidative degradation of ZDV by permanganate in acidic condition [24].

3.8. Effect of pH on the rate of the reaction

The effect of the variation in concentration of H^+ on the oxidative degradation of ZDV by permanganate was investigated in detail by varying concentration of buffer while keeping the concentration of ZDV and permanganate constant. Kinetics data show that there is decrease in the values of the rate constant with increase in the pH for the oxidative degradation of ZDV by permanganate reactions. It indicates that the oxidative degradation of ZDV by permanganate is faster in the acidic medium. The increase in the values of rate constant at lower value of pH may be due to increase in the concentration of active species of $HMnO_4$. The plot of apparent second-order rate constants k'_U vs. pH is shown in Fig. 7.

3.9. *Effect of temperature on the rate of the reaction*

The kinetics of oxidative degradation of ZDV by permanganate in acidic medium was studied systematically at temperatures 283, 288, 293, and 298 K by varying the concentration of ZDV from the range 5×10^{-4}–3.0×10^{-3} mol dm^{-3} while keeping other reaction conditions fixed. Experimental results show that the rate constants for oxidative degradation of ZDV by permanganate in acidic medium increases with a rise in the temperature from 283, 288, 293, and 298 K. The intercept of the plots of $1/k_{obs}$ vs. 1/[ZDV] at four different temperatures were used to obtain the values of the k (rate constant for the slow step) and these values are $2.43 \pm 0.14 \times 10^{-2}$ at 283 K, $4.56 \pm 0.17 \times 10^{-2}$ at 288 K, $5.22 \pm 0.22 \times 10^{-2}$ at 293 K, and $6.02 \pm 0.28 \times 10^{-2}$ at 298 K for the slow step reaction. Activation parameters such as E_a (kJ mol^{-1}), $\Delta H^{\neq}$ (kJ mol^{-1}), $\Delta G^{\neq}$ (kJ mol^{-1}), and $\Delta S^{\neq}$ (J K^{-1} mol^{-1}) were determined from the effect of variation in temperature using Arrhenius plot log k vs. $1/T$ ($R^2 > 0.999$) as shown in Fig. 8.

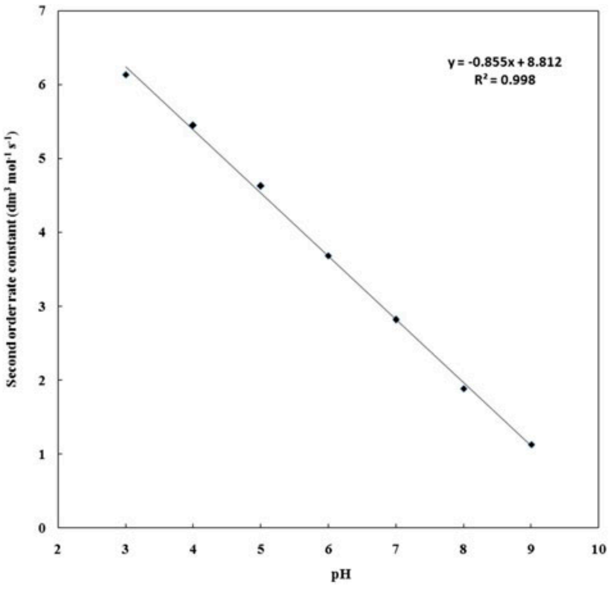

Fig. 7. pH-dependent apparent second-order rate constants for the oxidative degradation of ZDV by permanganate at different pH from 3.0 to 9.0 (298 K).

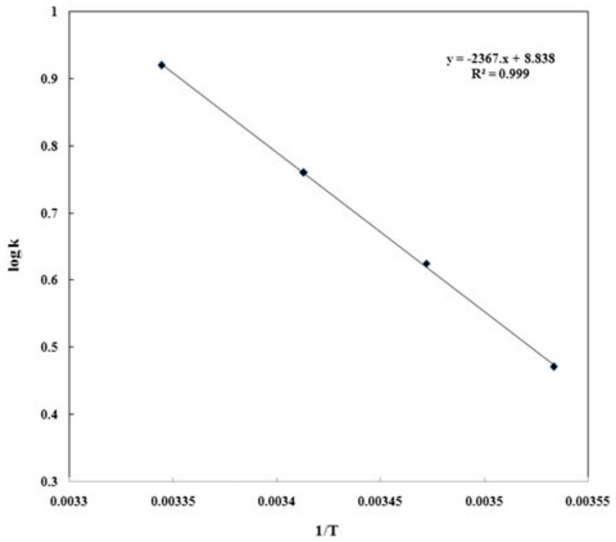

Fig. 8. Arrhenius plot log k vs. $1/T$ for four different temperatures 283, 288, 296, and 299 K by varying the concentration of ZDV from 5×10^{-4} to 3×10^{-3} mol dm^{-3}, while freezing other experimental conditions such as $[MnO_4^-] = 1 \times 10^{-4}$ mol dm^{-3}, [buffer] = 6×10^{-3} mol dm^{-3} and ionic strength (I) = 0.02 mol dm^{-3}.

4. Discussion

The values of the rate constants for oxidative degradation of ZDV by permanganate are found to be higher at lower pH. It indicates that $HMnO_4$ active species is dominant at lower pH. It means that at the higher concentration of H^+, the rate of formation of permanganic acid is more. In fact, $HMnO_4$ is the strongest oxidizing species of permanganate [25]. At the higher concentration of H^+ ion (at the lower pH) in the reaction mixture, the values of rate constants were tending to reach a limiting value after initial increase in the values of rate constants for the oxidative degradation of ZDV by permanganate in acidic medium. This clearly indicates that the protonation is completed at the lower pH and hence reaches to the limiting value. It implies that $HMnO_4$ is the only active species present in the reaction mixture in acidic condition. The rate constant values decreased rapidly with the increase in the pH of the reaction mixture, indicating that MnO_4^- is the dominant active species in neutral and alkaline medium. The chemical equilibrium which is established between MnO_4^- and $HMnO_4$ can be written as follows:

$$H^+ + MnO_4^- \overset{K_1}{\rightleftarrows} HMnO_4 \qquad (3)$$

In the above Eq. (3), K_1 is the equilibrium constant. The oxidative degradation of ZDV by permanganate in acidic medium indicates the first-order dependence for permanganate and fractional order dependence for the ZDV as well as H^+ ions.

HR-MS spectral analysis gives molecular ion peaks for the various degradation products of the oxidation of ZDV by permanganate in acidic medium. The molecular ion peak at m/z 290.08 is the sodiated peak for pure ZDV compound. Total eight products are identified with the help of observed molecular ion peaks from the HR-MS data. ZDV_P11 is the first product formed after degradation of ZDV by permanganate. Its molecular ion peak is observed at m/z 181.96 which is due to the fragmentation of ZDV under acidic condition and methyl group is oxidized to alcohol. ZDV_P21 s degraded product is identified at observed molecular ion peak at m/z 224.07. This ZDV_P21 is a thymine compound which is formed by the removal of azide group from the ring. The third degradation product is ZDV_P22 which is identified at molecular ion peak 239.91 m/z due to further oxidation of $–CH_2OH$ group of thymine to –COOH group. The fourth degradation product ZDV_P31 is identified at molecular ion peak 149.02 m/z as stavudine compound due to degradation of ZDV. The fifth degradation product ZDV_P32 is identified at molecular ion peak m/z 113.09 which is formed due to breaking of stavudine compound ring to form a compound containing two –CHO group. The sixth degradation product ZDV_P41 is identified at observed molecular ion peak m/z 140.90 due to degradation of ZDV. The seventh degradation product ZDV_P42 is identified at observed molecular ion peak m/z 114.05 due to removal of N_2 group from ZDV_P41. The eighth degradation product ZDV_P43 is identified at molecular ion peak m/z 130.90 which is formed due to further oxidation of $–NH_2$ group to –NHOH group. All these eight identified degraded products of ZDV by permanganate in acidic medium are listed in Table 1.

The kinetic data and HR-MS spectra are used to project a proposed mechanism of the oxidative degradation of ZDV by permanganate in acidic medium. In this proposed mechanism, experimental observed orders for the concentration of ZDV, concentration of permanganate, and $[H^+]_f$ are taken into consideration. In this proposed mechanism, the first equilibrium is established between MnO_4^- ion and permanganic acid. K_1 is the equilibrium constant for the first equilibrium step which shows the formation of permanganic acid. Then, in the next step, there is a formation of stable complex *C* between ZDV and permanganic acid. K_2 is the equilibrium constant for the formation complex *C* between ZDV and permanganic acid. This complex *C* in the slow step forms an intermediate compound. The rate constant for this slow step of intermediate compound formation is *k*. Then, the intermediate compound gives eight degraded products in which Mn^{7+} is reduced to Mn^{6+} and forms oxidized product in the fast step. Further in next fast step, Mn^{6+} is reduced to Mn^{5+} along with formation of oxidized products. Subsequently, in the next fast step, Mn^{5+} reduces to Mn^{4+} after the degradation of intermediate compound. Finally, Mn^{4+} is reduced to form Mn^{2+} along with the formation of oxidized products. The results may be interpreted as per the Fig. 10. As per the literature survey, there are many previous investigations which show the same steps involved in the Fig. 10 for the oxidative degradation reactions [26].

The oxidative degradation of ZDV by permanganate in acidic medium formed a complex between ZDV and permanganic acid for the concentrations of ZDV = 1×10^{-3} mol dm^{-3} and permanganate = 1.0×10^{-4} mol dm^{-3}. This is supported by spectra obtained from UV–vis spectrophotometer.

The straight line plot of $1/k_{obs}$ vs. 1/[ZDV] (Michaelis–Menton plot as shown in Fig. 9) having the positive intercept confirms that the complex *C* is formed between ZDV and permanganic acid. A literature

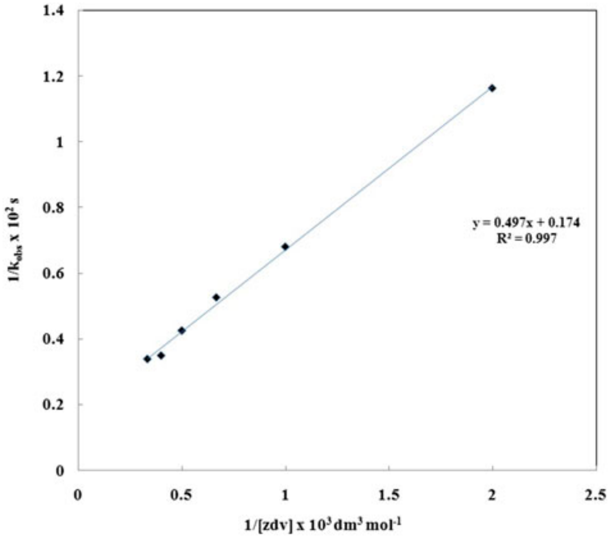

Fig. 9. Plot of $1/k_{obs}$ vs. 1/[ZDV] for the oxidative degradation of ZDV by permanganate in acidic medium at 298 K for the verification of the rate law. [ZDV] = 5×10^{-4} to 3×10^{-3} mol dm^{-3}, $[MnO_4^-] = 1 \times 10^{-4}$ mol dm^{-3}, [buffer] = 6×10^{-3} mol dm^{-3}, ionic strength (*I*) = 0.02 mol dm^{-3}.

survey also reported such type of complex formation between substrate and permanganic acid.

The rate law equation (Eq. (8)) for the mechanism of oxidative degradation of ZDV by permanganate in acidic medium can be obtained as per Fig. 10 (See Appendix 1 for Eqs. (4)–(7)).

$$\text{Rate} = \frac{-\mathrm{d}[\mathrm{MnO_4^-}]}{\mathrm{d}t} = \frac{\mathrm{k\,K_1K_2}\left[\mathrm{MnO_4^-}\right][\mathrm{ZDV}][\mathrm{H^+}]}{1 + \mathrm{K_1[H^+]} + \mathrm{K_1\,K_2[H^+][ZDV]}} \tag{8}$$

$$\frac{\text{Rate}}{[\mathrm{MnO_4^-}]} = \mathrm{k_{obs}} = \frac{\mathrm{k\,K_1\,K_2}\left[\mathrm{MnO_4^-}\right][\mathrm{ZDV}][\mathrm{H^+}]}{1 + \mathrm{K_1[H^+]} + \mathrm{K_1\,K_2[H^+][ZDV]}} \tag{9}$$

The rate law Eq. (9) can be rearranged into the following form:

$$\frac{1}{\mathrm{k_{obs}}} = \frac{1}{\mathrm{k\,K_1K_2[ZDV][H^+]}} + \frac{1}{\mathrm{k\,K_2[ZDV]}} + \frac{1}{\mathrm{k}} \tag{10}$$

As per the above given Eq. (10), by keeping other conditions constant, plots of $1/\mathrm{k_{obs}}$ vs. $1/[\mathrm{ZDV}]$ and $1/\mathrm{k_{obs}}$ vs. $1/[\mathrm{H^+}]$ should be linear. This was verified from the plot of $1/\mathrm{k_{obs}}$ vs. $1/[\mathrm{ZDV}]$. Values of k, $\mathrm{K_1}$, and $\mathrm{K_2}$ are obtained as $6.02 \times 10^{-2}\ \mathrm{dm^3\,mol^{-1}\,s^{-1}}$, $38\ \mathrm{dm^3\ mol^{-1}}$, and $1.487 \times 10^3\ \mathrm{dm^3\ mol^{-1}}$ at 298 K, respectively, from the slopes and intercepts of these plots. The above obtained $\mathrm{K_1}$ value is found to be in good agreement with the literature [27]. Using these constants, the rate constants were calculated and compared with the experimental $\mathrm{k_{obs}}$ values. There was a reasonable agreement with each other which supports the proposed mechanism as shown in Fig. 10.

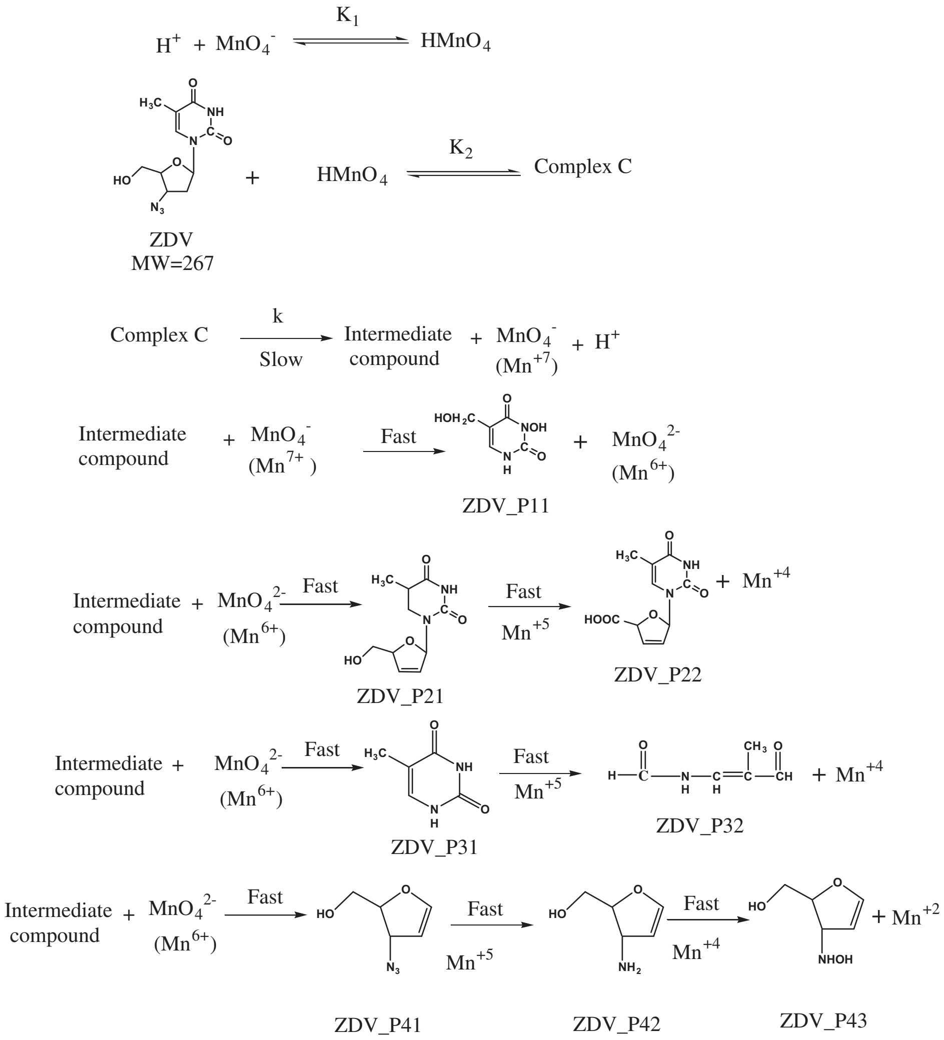

Fig. 10. The plausible mechanism of the oxidative degradation of ZDV by permanganate in acidic medium.

From the linear Arrhenius plot of log k vs. $1/T$, the activation energy was calculated. With the help of the energy of activation, values of the other activation parameters such as enthalpy of activation, entropy of activation, and Gibbs free energy of activation were calculated. The result shows that the average value of energy of activation energy (E_a) was found to be 45.32 kJ mol^{-1}, entropy of activation $\Delta S^{\neq}$ was found to be −135.44 JK^{-1} mol^{-1}, and free energy of activation ($\Delta G^{\neq}$) was found to be 82.29 kJ mol^{-1} but the value of enthalpy of activation ($\Delta H^{\neq}$) was found to be 42.91 kJ mol^{-1}. The value of entropy of activation is found to be negative. The high negative value of $\Delta S^{\neq}$ suggests that the formation of more activated complex, whereas the high positive value of the free energy of the activation ($\Delta G^{\neq}$) and enthalpy of activation ($\Delta H^{\neq}$) indicate that the transition state is highly solvated. Energy of activation, free energy of activation, and entropy parameters suggest that permanganic acid forms the activated complex more easily compared to the other oxidants. Mechanism consistent with observed rate laws have been suggested. The values of free energy of reaction $\Delta G^{\neq}$, enthalpy of reaction $\Delta H^{\neq}$, and entropy of reaction $\Delta S^{\neq}$ were calculated for the first and second equilibrium steps. A comparison of the later values (from K_2) with those obtained for the slow step of the reaction shows that these values mainly refer to the rate-limiting step, supporting the fact that the reaction before rate-determining step is fairly fast and involves low activation energy [28,29].

The ionic strength (I) has no significant effect on the rate constant of the redox reaction. During an experiment, it is observed that there is no reaction between the oxidizing agent and solvent. This indicated that negligible effect of variation in ionic strength on the rate of reaction explains the reaction is between two neutral species or a neutral and a charged species [30]. The effect of dielectric constant shows that the reaction is between two dipoles as explained by Amis [31].

5. Conclusion

The oxidative degradation of ZDV by permanganate in the acidic medium was studied in detail. ZDV is an antiretroviral drug which has been used as a model pharmaceutical compound for the oxidative degradation. In this oxidative degradation, the active species of permanganate are found permanganic acid. In this study, it is observed that acidic medium plays a vital role in oxidative degradation of ZDV by permanganate. The whole sequence described in this investigation is in agreement with oxidative degraded products formed and projected mechanism. The rate constant for the slow step (k) as shown in Fig. 10 and other equilibrium constants K_1 and K_2 are calculated. From the effect of variation in temperature on the rate of reaction, the activation parameters for the slow step are also calculated. The calculated value of change in entropy is found to be negative which implies that formation of more activated complex takes place between the substrate ZDV and permanganic acid. Free energy of activation and enthalpy of activation are also calculated. The positive values of these two terms ΔG and ΔH implies that the solvation of transition state is very high. The plausible mechanism for the oxidative degradation by permanganate in acidic medium is consistent with the experimental results obtained. The rate law is derived for the oxidative degradation by permanganate in acidic medium. This mechanistic insight into the oxidative degradation by permanganate in acidic medium clearly indicates that permanganate acts as an efficient oxidant to degrade the emerging contaminant ZDV present in the water.

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Appendix 1

The rate law for the oxidative degradation of ZDV by permanganate in acidic medium for Fig. 10 can be obtained as follows:

$$\text{Rate} = \frac{-\mathrm{d}[\mathrm{MnO_4^-}]}{\mathrm{d}t} = \mathrm{k}\,[\text{Complex C}]\,[\mathrm{HMnO_4}]$$

$$\text{Rate} = \frac{-\mathrm{d}[\mathrm{MnO_4^-}]}{\mathrm{d}t} = \mathrm{k\,K_1\,K_2}[\mathrm{ZDV}]_\mathrm{f}\,[\mathrm{MnO_4^-}]_\mathrm{f}[\mathrm{H^+}]_\mathrm{f} \tag{4}$$

Now, $[\mathrm{MnO_4^-}]_\mathrm{T}$ can be written as:

$$[\mathrm{MnO_4^-}]_\mathrm{T} = [\mathrm{MnO_4^-}]_\mathrm{f} + [\mathrm{HMnO_4}] + [\text{Complex C}]$$

$$= [\mathrm{MnO_4^-}]_\mathrm{f} + \mathrm{K_1}[\mathrm{H^+}][\mathrm{MnO_4^-}]_\mathrm{f} + \mathrm{K_1\,K_2}[\mathrm{ZDV}][\mathrm{H^+}][\mathrm{MnO_4^-}]_\mathrm{f}$$

$$= [\mathrm{MnO_4^-}]_\mathrm{f}\{1 + \mathrm{K_1}[\mathrm{H^+}] + \mathrm{K_1\,K_2}[\mathrm{H^+}][\mathrm{ZDV}]\}$$

In the above equations, T and f indicate total and free concentrations.

$$[\mathrm{MnO_4^-}]_f = \frac{[\mathrm{MnO_4^-}]_T}{1 + K_1[\mathrm{H^+}] + K_1 K_2[\mathrm{H^+}][\mathrm{ZDV}]} \tag{5}$$

Similarly,

$$[\mathrm{H^+}]_T = [\mathrm{H^+}]_f + [\mathrm{HMnO_4}]$$

$$= [\mathrm{H^+}]_f + K_1[\mathrm{H^+}][\mathrm{MnO_4^-}]$$

As the concentration of H^+ ions is low in the reaction mixture, the term K_1 $[H^+]$ $[[HMnO_4]$ can be neglected from the above equation. Hence, the above equation becomes:

$$[\mathrm{H^+}]_T = [\mathrm{H^+}]_f \tag{6}$$

In the same way, the total concentration of ZDV can be written as,

$$[\mathrm{ZDV}]_T = [\mathrm{ZDV}]_f \tag{7}$$