Spectroscopic Studies on the Dynamics of Charge-Transfer Interaction of Pantoprazole Drug with DDQ and Iodine

M. PANDEESWARAN,[1] E. H. El-MOSSALAMY,[2] K. P. ELANGO[1]

[1]*Department of Chemistry, Gandhigram Rural University, Gandhigram 624 302, India*
[2]*Chemistry Department, King Abdul Aziz University, Jeddah 21589, Saudi Arabia*

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ABSTRACT: Spectrophotometric method was used to study the kinetics of charge-transfer (CT) complexes of pantoprazole with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and iodine. The reactions of DDQ and iodine with pantoprazole have been investigated in different solvents at three different temperatures. The products of the interactions have been isolated and characterized using UV–vis, GC-MS, FT-IR, and far-IR spectral techniques. The rate of formation of the product has been measured and discussed as a function of solvents and temperature. The iodine complex indicates the formation of the tri-iodide CT complex with a general formula $[(PTZ)I]^{+}I_3^{-}$. The characteristic strong absorptions of I_3^{-} are observed around 360 and 290 nm in the electronic spectra, and the far-IR spectrum exhibits three characteristic vibrations of I_3^{-} unit at 156, 112, and 69 cm^{-1} assigned to ν_{as}(I-I), ν_s(I-I), and $\delta(I_3^{-})$, respectively. The activation parameters ($\Delta G^{\#}$, $\Delta S^{\#}$, and $\Delta H^{\#}$) were obtained from the temperature dependence of the rate constants. The influence of relative permittivity of the medium on the rate indicated that the intermediate is more polar than the reactants, and this observation was further well supported by spectral studies. Based on the spectrokinetic results, plausible mechanisms for the interaction of the drug with the chosen acceptors, which proceed via the formation of CT complexes and its transformation into final products, have been proposed. © 2009 Wiley Periodicals, Inc. Int J Chem Kinet 41: 787–799, 2009

INTRODUCTION

For the past several years, exhaustive studies have been carried out on the molecular interactions between electron donors and acceptors [1–16]. During the recent past, considerable attention has been directed toward finding the possible role of electron donor–acceptor complexes or charge-transfer (CT) complexes

Correspondence to: K. P. Elango; e-mail: drkpelango@rediffmail.com.

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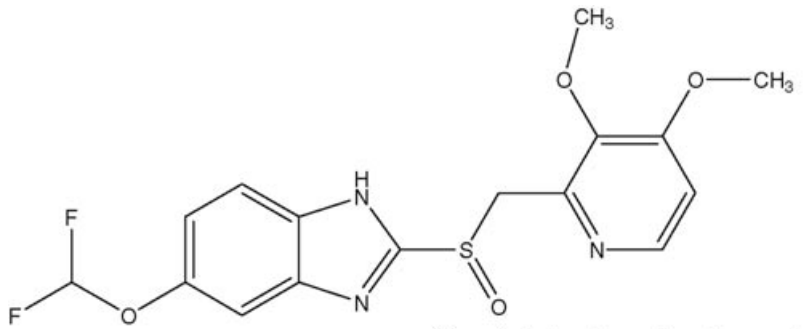
in chemical reactions [17,18]. Although CT complexes are currently of immense importance in analytical chemistry, material science and technology [5,19], and subject of analysis by recent theoretical calculations [20], they also play significant role in biological and bio-electrochemical energy and CT processes [21]. However, studies on the kinetics of such reactions involving drug molecules are relatively fewer in number. We are interested in the spectrokinetic studies on the CT interactions of drugs with different types of electron acceptors. Therefore, in continuation of our earlier works on the spectrokinetic studies on the interaction of drug molecules such as povidone, ketoconazole, atenolol, and dextromethorphan with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and iodine [22–25], here in this article we report the spectroscopic (far IR, UV–vis, GC-MS, etc.) studies on the dynamics of the interaction of pantoprazole (PTZ) drug with an π-acceptor, DDQ, and an σ-acceptor, iodine.

Quinones and iodine are well known for their electron-accepting properties. Iodine is being used as a model acceptor to investigate the electron-donating properties of organic molecules [26]. In human biology, iodine is required for the biosynthesis of the thyroid hormones, tri-iodothyonine, and thyroin, which regulate metabolic rate [27,28]. Likewise, the studies of quinones for their CT interaction stem from their possible role in biological reactions. Quinones are also known to be important in many biological fields [29,30]. Thus, the mechanism of interaction of iodine and quinones with drugs, in general, is a research topic of significant interest and hence the present study. Furthermore, it is also to be noted that most of the studies on the CT complexes are reported in nonpolar solvents whereas the present study has been attempted in a wide range of relative permittivity of the medium with an aim to study the effect of solvent on the interaction dynamics.

EXPERIMENTAL

Material and Methodology

The electron acceptors DDQ (minimum assay 98%) and iodine (minimum assay 99.9%) were obtained from Aldrich (Bangalore, India) and were used as received. Commercially available spectroscopy grade solvents (Merck, Mumbai, India) were used without further purification. The selection of the solvents is based on the solubility of the components and so as to have a wide range of relative permittivity of the medium. The electron donor drug, PTZ, was obtained as gift sample from locally available pharmaceutical company. As it is certified as pure, we have used as received. Furthermore, the purity of the drug was also checked by comparing the FT-IR spectrum with that reported. The structure of the donor drug is shown below.



Chemical structure of pantoprazole

Solutions for the spectroscopic measurements were prepared by dissolving accurately weighed amounts of donor (D) and acceptor (A) in the appropriate volume of solvent immediately before running the spectra. The electronic absorption spectra are recorded on a Shimadzu (UV 240, Graphicord) double beam spectrophotometer using 1-cm matched quartz cells. The temperature of the cell holder was controlled with a water flow ($\pm$0.2°C). FT-IR spectra were recorded in a JASCO FT/IR-460Plus spectrometer. Far-IR spectra of the reaction product were obtained from SAIF, Indian Institute of Technology, Chennai, India. GC-MS spectra were obtained from the Central Salt and Marine Research Institute, Bhavanagar, India. The conductance of the solutions was measured on an Elico, India, conductivity bridge. For the conductance measurements, equimolar stock solutions of D and A were thermostated to a constant temperature and were mixed in the conductivity cell by varying the mole fraction of A. The solutions were stirred after each addition and a constant time interval was permitted to record the conductance.

Kinetic Procedure

In both PTZ–I_2 and PTZ–DDQ systems, the kinetics was followed under pseudo-first-order conditions keeping [D] ≫ [A] at three different temperatures in various solvents. The increase in absorbance of the peak around 400 nm in the case of DDQ and around 360 nm in the case of iodine (depending on the solvent) was followed as a function of time. The pseudo-first-order rate constants (k_1) were calculated from the gradients of log ($A_\infty - A_t$) against time plots, where A_∞ and A_t represent the absorbance at infinity and time t, respectively. The second-order rate constants (k_2) were calculated by dividing k_1 by [D].

RESULTS AND DISCUSSION

Stoichiometry of the Reaction

The stoichiometry of the CT complexes was determined by applying Job's continuous variation method [31]. In both the cases, the symmetrical curves with a maximum at 0.5 mol fraction indicated the formation of a 1:1 (D:A) CT complex (figure not shown). The photometric titration measurements were also performed to confirm the stoichiometry. The [D] in the reaction mixtures was kept constant, whereas [A] was varied over a wide range. The results of the photometric titration (Fig. 1) indicated that the stoichiometry, in both cases, is 1:1 (D:A) [32].

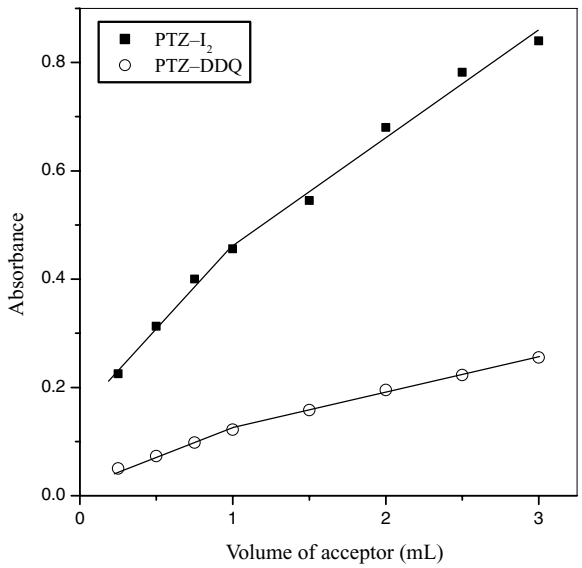


Figure 1 Photometric titration curves for the interaction of PTZ with iodine (358 nm) and DDQ (400 nm) in *tert*-butyl alcohol at 298 K.

Table I Infrared Wavenumber (cm^{-1}) and Tentative Band Assignments for the PTZ, PTZ—DDQ, and PTZ–I_2 Complexes

PTZ	PTZ–DDQ	PTZ–I_2	Assignments
3489m	3407b	3434b	ν(—OH);
3184b	–	3073w	ν(N—H);
2995m	2925s	2932m	ν(C—H); aliphatic
2842w	2855w	2843w	
	2226m		ν(C≡N); DDQ
	2203s		
	1679s		ν(C═O); DDQ
			ν(C═C); DDQ
1652w	1621w	1622m	ν(C═O);
1590s	1578s	1577m	ν(C═C); aromatic
1451m	1448m	1436w	ν(S═O); asymmetric
1376s	1385m	1385m	ν(C—N); aromatic
1231w	1244w	1231w	ν(Ar—O—CH_2)
1167s	1173m	1168m	ν(S═O); symmetric
1039s	1033m	1039m	ν(C—O); aromatic ether
817m	828m	824m	ν(C—F);
	799s		ν(C—Cl); DDQ
	771w		
746,711	707	746w, 713w	ν(C—S); aliphatic
			ν(N—H); wagging and aliphatic methylene rock

s, strong; m, medium; w, weak; b, broad; ν, stretching.

Interaction of Pantoprazole with Iodine

The reaction product was obtained by allowing the reactants to react for 24 h under equal molar conditions in 1,2-dichloroethane and subjected to MPLC separation. The FT-IR spectra of the product and pure D were recorded, and the peak assignments for important peaks are given in Table I. From the results, it is evident that on comparing the FT-IR spectrum of pure PTZ, that of the product showed shifts in many peak positions. Some of the significant shifts are the peak due to ν(N—H) vibrations of the free PTZ occurs at 3184 cm^{-1} and in iodine complexes it appeared at 3073 cm^{-1}. The ν(S═O) asymmetric, ν(C—F), and ν(C═C) vibrations of the free PTZ occur at 1451, 817, and 1590 cm^{-1}, and in the iodine complex they appeared at 1436, 824, and 1577 cm^{-1}, respectively. The results indicated that the shifts in positions of some of the peaks could be attributed to the expected symmetry and electronic structure modification in both D and A units in the formed product relative to the free molecules.

The far-infrared spectrum of the PTZ–I_2 complex is shown in Fig. 2, and the spectral data are collected in Table II. The spectrum showed the characteristic bands of the I_3^- ion at 156, 112, and 69 cm^{-1}. It is well known that the I_3^- ion exists as one unit with either linear

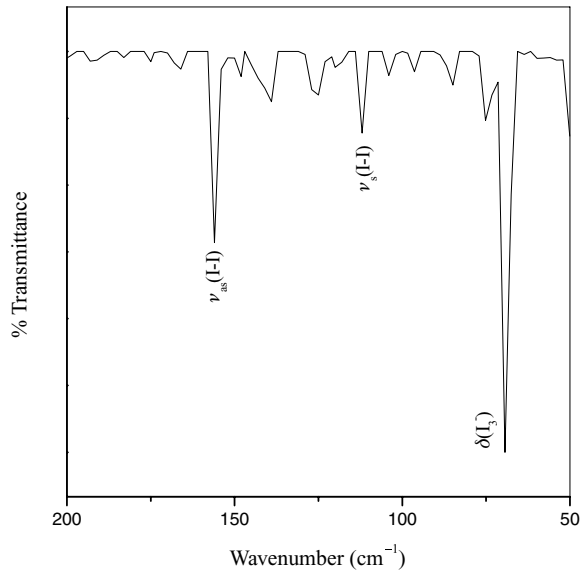


Figure 2 Far-infrared spectrum of $[(PTZ)I]^+I_3^-$.

Table II Fundamental Vibrations for I_3^- Ion

	Assignments			
Compound	ν_{as}(I-I)	ν_s(I-I)	$\delta(I_3^-)$	Reference
Povidone	147	104	86	[24]
Ketoconazole	158	114	86	[24]
[(DAPY)I] I_3^-	151	132	61	[13]
$[Fe(acac)_3]_2\ I^+\ I_3^-$	150	102	76	[34]
[(HMTACTD)I] I_3^-	144	110	60	[33]
[(PTZ)I] I_3^-	156	112	69	Present work

or bent structures [13]. The group theoretical analysis showed that the three vibrations should be infrared active. The 156 cm^{-1} is assigned to the antisymmetric stretch of the I-I bond, ν_{as}(I-I). The corresponding symmetric stretch, ν_s(I-I), is observed at 112 cm^{-1}. The band at 69 cm^{-1} is assigned to the bending vibration, $\delta(I_3^-)$ [33,34]. These assignments are exactly similar to those known for the nonlinear I_3^- ion. The results in the present study, therefore, indicated the presence of nonlinear tri-iodide ion in the PTZ–I_2 complex.

On mixing *tert*-butyl alcohol solutions of PTZ and iodine, there was an instantaneous formation of lemon yellow color with a new absorption maxima centered at 358 nm in the UV–vis spectrum (Fig. 3), where neither the D nor the A absorbs measurably. Such an observed variation in the electronic spectrum of the mixture indicated the interaction between the D and A. The absorption band around 460 nm, which is attributed to the π–σ^* electronic transition in free iodine, is hypsochromically shifted due to its complexation with the D. The observed hypsochromic shift in the free iodine band could be attributed to the perturbation of the iodine molecular orbital σ^* by a repulsive complex. Accordingly, a more repulsive interaction would lead to a large blue shift of the iodine band. Therefore, it is reasonable to consider the extent of the blue shift in iodine band as a measure of the magnitude of interaction between the D and iodine molecules. The limiting value of this shift is at 350 nm, which is the characteristic absorption of the I_3^- ion in solution. Thus, as indicated by the far-IR spectral study, the PTZ–I_2 complex contains tri-iodide ion moiety in it. Parallel

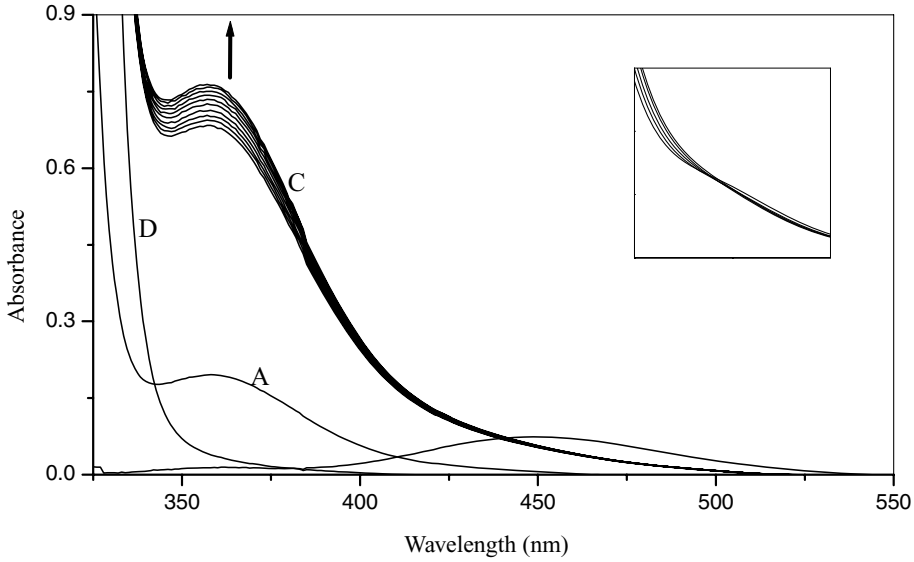


Figure 3 Absorption spectra of PTZ with iodine in *tert*-butyl alcohol at 298 K; [D] = 5.6625×10^{-3} M and [A] = 3.7235×10^{-5} M. (Insert shows the isosbestic point at 444 nm.)

Table III Effect of Concentration of Donor and Acceptor on the Rate of Product Formation

10^3 [D] (M)	10^5 [A] (M)	10^4 k_1 (s^{-1})	10^2 k_2
Pantoprazole–DDQ (in *tert*-butyl alcohol at 400 nm)			
2.37	6.61	1.12	4.7
3.56	6.61	1.75	4.9
4.74	6.61	2.08	4.4
5.93	6.61	2.72	4.6
5.93	6.61	2.72	
5.93	5.29	2.70	
5.93	3.96	2.68	
5.93	2.64	2.69	
Pantoprazole–iodine (in *tert*-butyl alcohol at 358 nm)			
0.80	4.92	0.52	6.5
1.20	4.92	0.77	6.4
1.60	4.92	1.05	6.6
2.00	4.92	1.34	6.7
2.00	4.92	1.34	
2.00	3.94	1.36	
2.00	2.96	1.33	
2.00	1.97	1.37	

observations were made by us and several other investigators in the study of molecular complexes of iodine with various donors [35,36].

Furthermore, the spectrum (Fig. 3) of the mixture of PTZ and iodine is time dependent, and the intensity of the characteristic I_3^- ion band at 358 nm increased with lapse of time. Consequently, the change in absorbance of the solution, at 358 nm, was measured as a function of time to evaluate the rate constants for the interaction. A clear isosbestic point was observed at 444 nm, indicating a decrease in the concentration of free iodine molecule. However, no attempt was made to measure the decrease in intensity of the peak as it becomes constant quickly in majority of the solvents. The observed time dependence of the electronic spectra of the system under investigation is due to a transformation of the initially formed outer complex (CT complex) into an inner complex followed by a fast reaction of the resulting inner complex with iodine to form a tri-iodide ion, as depicted below [35–37]. As evidenced from FT-IR spectral studies, the point of attachment of PTZ with iodine is the NH moiety of the drug.

$$\text{Drug} + I_2 \rightleftharpoons \text{Drug} - I_2(\text{outer complex}) \quad \text{Fast} \tag{1}$$

$$\text{Drug} - I_2 \rightleftharpoons [\text{Drug} - I]^+I^-(\text{inner complex}) \quad \text{Slow} \tag{2}$$

$$[\text{Drug} - I]^+I^- + I_2 \rightleftharpoons [\text{Drug} - I]^+I_3^- \quad \text{Fast} \tag{3}$$

The pseudo-first-order rate constants, k_1, as a function of [D] and [A] are given in Table III. The results indicated that the pseudo-first-order rate constants were independent of initial concentrations of the acceptor, indicating first-order dependence in [A]. The k_1 increased with an increase in [D], and a plot of log k_1 versus log [D] is linear ($r = 0.999$) with a slope of 1.03 ± 0.02, indicating first-order dependence on [D] and the same of confirmed by constant k_2 values.

The rate constants as a function of temperature and solvent along with activation parameters for the PTZ–I_2 interaction are collected in Table IV. The results indicated that the k_1 values increased with an increase in the relative permittivity of the medium. A plot of log k_1 versus ε_r is shown in Fig. 4. It is evident from the figure that there is deviation from linearity especially at higher relative permittivity values. This may be due to the fact that with an increase in polarity of the medium solvent–solvent interaction becomes increasingly significant in addition to solute–solvent interactions [22]. This solvent dependence of the k_1 values suggested that there may be some charge separation in the transformation of CT complex to the final product. Formation of such a more polar transition state is well supported by the large negative entropy of activation values [22]. Furthermore, negative entropy of activation indicates a greater degree of ordering in the transition state than in the initial state, due to an increase in solvation during the activation process. The positive

Table IV Kinetic and Thermodynamic Parameters for the Reaction of Iodine with PTZ

			10^3 k_1 (s^{-1})					
Solvent	ε_r	λ(nm)	298 K	305 K	313 K	$\Delta H^{\#}$ (kJ mol^{-1})	$\Delta S^{\#}$ (J $K^{-1}mol^{-1}$)	$\Delta G^{\#}$ (kJ mol^{-1})
Chloroform	4.90	361	0.18	2.30	6.52	181	292	93.6
tert-Butyl alcohol	12.47	358	0.21	1.32	4.08	151	192	93.7
Methanol	32.70	359	1.29	1.83	4.01	50	−112	89.7
DMF	36.71	525	2.30	4.84	5.67	44	−148	87.8

ε_r, Relative permittivity of the medium.

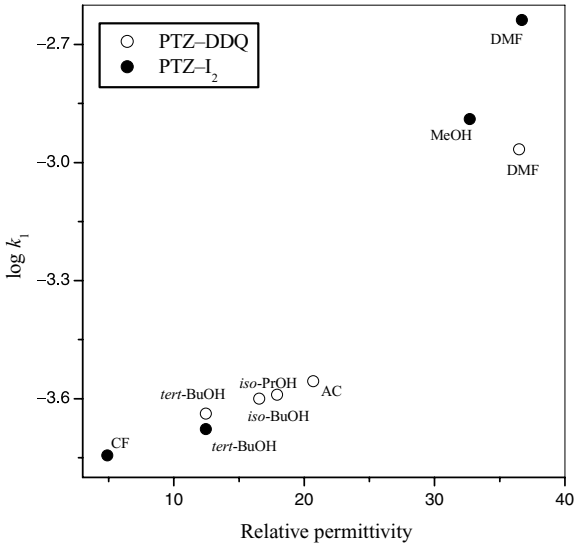


Figure 4 Plot of log k versus relative permittivity of the medium.

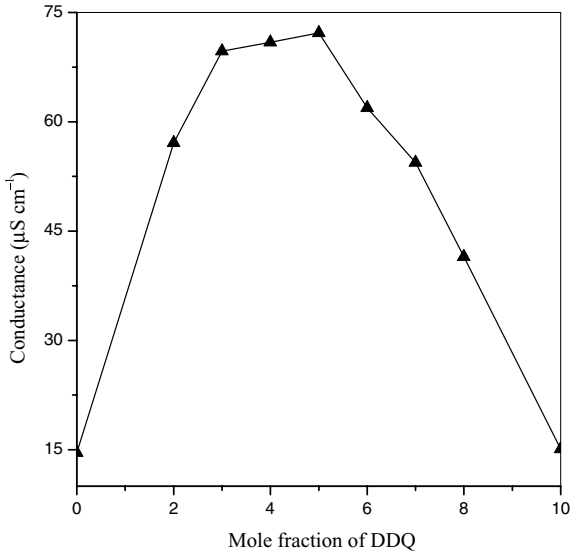


Figure 6 Conductivity versus mole fraction of DDQ plot of PTZ–DDQ system in *tert*-butyl alcohol at room temperature.

values of enthalpy of activations indicated the endothermic nature of the interaction between the D and the A. There exists linear correlation (Fig. 5; $r = 0.999$) between $\Delta H^{\#}$and $\Delta S^{\#}$ values, indicating the operation of a common mechanism in all the solvents studied. A perusal of data in Table IV indicated that a solvent change from chloroform to DMF caused a ∼32-fold rate acceleration for the reaction, which corresponds to a decrease in $\Delta G^{\#}$ of 6 kJ mol^{-1}.

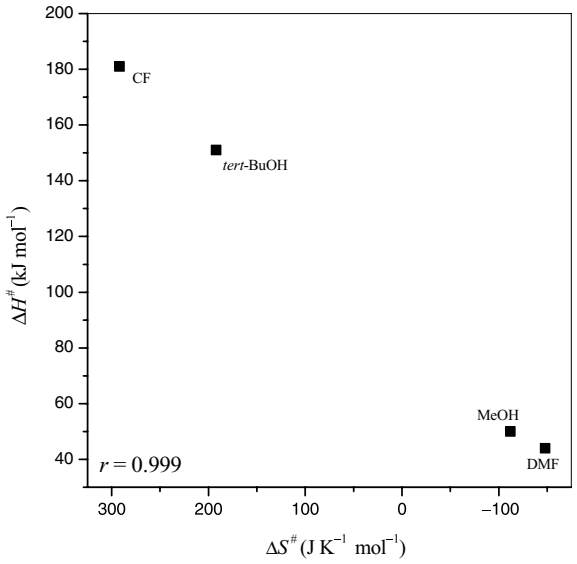
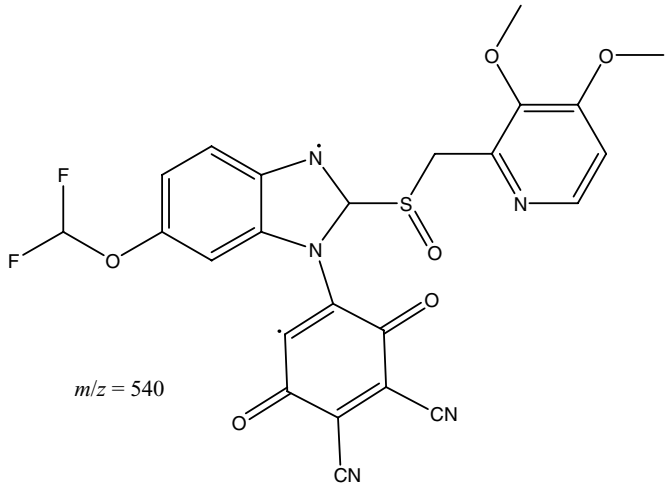


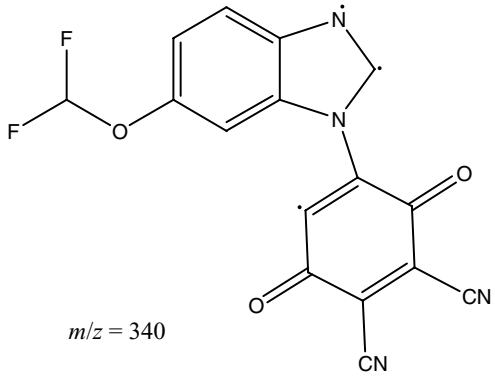
Figure 5 Relation between enthalpy and entropy of activations for the interaction of PTZ with iodine.

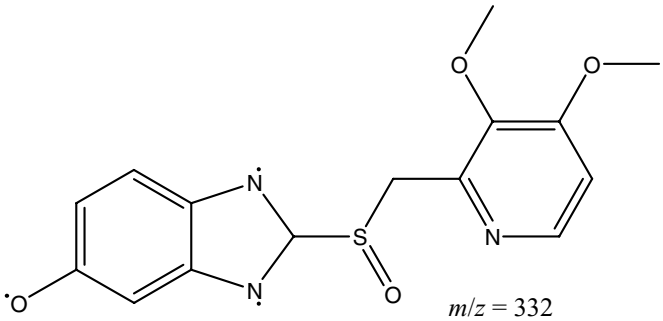
Interaction of Pantoprazole with DDQ

In the case of PTZ–DDQ system, the characterization of the reaction product was done using FT-IR and GC-MS techniques. For that the product was obtained by allowing the reactants to react for 24 h under equal molar conditions in acetonitrile and subjected to MPLC separation. The peak assignments for important peaks in the FT-IR spectra are also given in Table I. The results indicated that the shifts in positions of some of the peaks could be attributed to the expected symmetry and electronic structure modification in both D and A units in the formed products relative to the free molecules. Some of the significant shifts are the peak due to ν(N—H) vibrations of the free PTZ occurs at 3184 cm^{-1} and in the product it disappeared suggesting the involvement of the N—H group of the drug in the interaction with DDQ. The ν(S═O) asymmetric, ν(C—F), and ν(C═C) vibrations of the free PTZ occur at 1451, 817, and 1590 cm^{-1}, and in the product they appeared at 1448, 828, and 1578 cm^{-1}, respectively. The ν(C═O), ν(C≡N), and ν(C—Cl) stretching vibrations in the DDQ species appeared at 1679, 2226, and 799 cm^{-1}, respectively. In the product, these stretching vibrations occurred at 1621, 2203, and 771 cm^{-1}, respectively. Such a bathochromic shift could be indicative of a higher charge density on the carbonyl and cyano groups of the DDQ molecule [22].

The mass spectrum of the product displayed the following important peaks at m/z values corresponding to the structure of the fragments of the product.







Conductimetry has been often employed to study the interactions of CT complexes [38–40]. In the present study, a mixture of *tert*-butyl alcohol solutions of PTZ and DDQ exhibits appreciable conductivities, which may be due to the formation of a CT complex. The increase in conductivity observed upon the CT complex formation may be due to the fact that the CT complex formed between D and A may undergo dissociation into ionic intermediate in solvents of sufficient high relative permittivity give rise to appreciable conductivity [22,41]. The conductivity–mole fraction plot yielded maximum at a D:A molar ratio of 1:1 as evidenced from Fig. 6.

$$D + A \rightleftarrows DA \tag{4}$$

$$DA \rightleftarrows [D^{+}A^{-}] \tag{5}$$

The electronic absorption spectra of DDQ in the presence of a large excess of the donor, i.e., $[D]/[A] > x$ was obtained as a function of time in different solvents. The representative electronic absorption spectra of the mixture of PTZ and DDQ in acetone showed a group of absorption bands at 509, 546, and 590 nm (Fig. 7). These absorption bands are characteristic for the absorption of the radical anion $DDQ^{-\bullet}$ [4,8,42,43]. The observed enhanced absorption band intensities, immediately after mixing D and A, supports the fact that the CT complex formed is of the dative-type structure, which consequently converts to an ionic intermediate possessing the spectral characteristics of radical anion [23]. Furthermore, the observed gradual decrease in the intensity of the bands in the 500–600-nm spectral regions, with lapse of time, could be due to the consumption of the ionic intermediate through an irreversible chemical reaction. While the continuous increase of the 433-nm band with lapse of time is indicative of the formation of the final reaction product [44]. Such a conversion of the dative intermediate to product is indicated by a clear isosbestic point at 495 nm.

The nature of the intermediate formed in the interaction between PTZ and DDQ was also identified using the following experiment. Chloroform solutions of the A and the D were extracted separately with water and were mixed together. The electronic spectrum of the mixture, recorded immediately after mixing the water extracts, is shown in curve C_1 of Fig. 8. It is observed that there was no appreciable change in the absorption spectrum of the mixture even after 24 h (curve C_2), which indicated that there is no reaction between the A and the D in aqueous medium. The chloroform solutions of the acceptor and donor were mixed together,

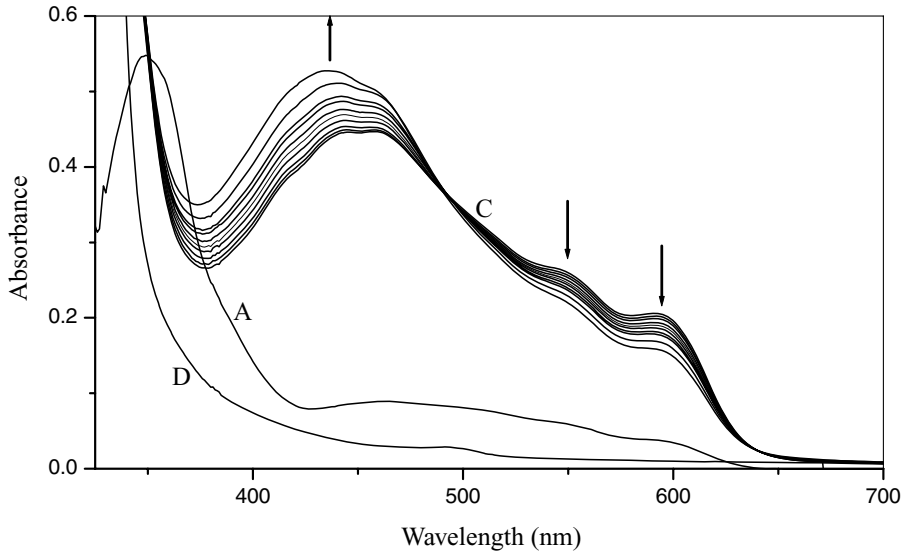


Figure 7 Absorption spectra of PTZ with DDQ in acetone at 298 K; [D] = 1.8947×10^{-2} M and [A] = 1.6096×10^{-4} M.

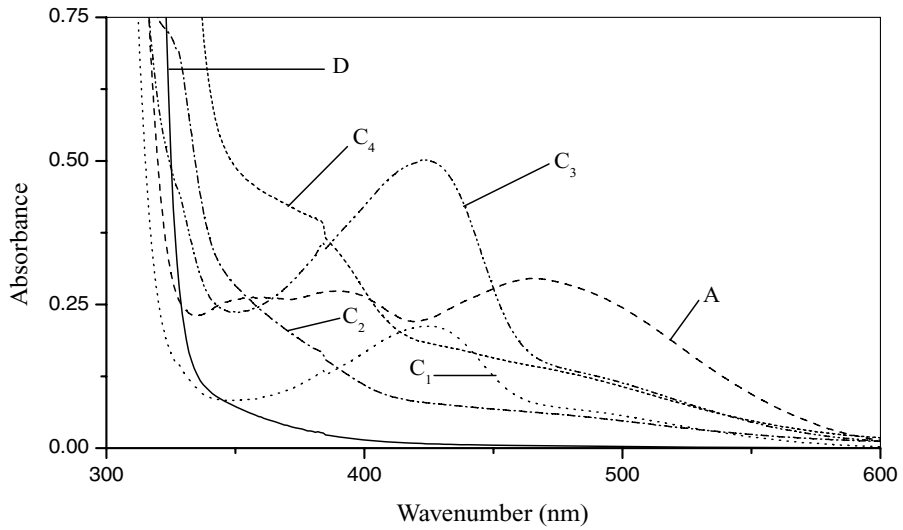


Figure 8 Absorption spectra for the interaction of PTZ with DDQ.

and the brown-colored solution thus obtained was extracted with water. The absorption spectrum of the extract, recorded immediately, is shown by curve C_3. The curve C_3 closely resembles that of the reaction product as shown in Fig. 8. This observation suggests the formation of a polar intermediate in the interaction between PTZ and DDQ that is converted into the final product [45].

To obtain further information about the kinetics and mechanism of the reaction of DDQ with PTZ, the increase in absorbance of the band around 400 nm (depending on the solvent) was monitored as a function of time in different solvents under pseudo-first-order conditions, keeping large excess of [D] over [A]. The pseudo-first-order rate constant (k_1) values for the formation of the reaction product as a function of [D] and [A] are also collected in Table III. It is evident from the results that the rate is independent of initial concentration of [A], indicating first-order dependence on [A]. The rate constant values increased with an increase in [D], and a plot of log k_1 versus log [D] is linear ($r = 0.994$) with a slope of 0.94 ± 0.07, indicating first-order dependence of the rate on [D] and which was further supported by the constancy in k_2 values.

The effect of solvent on the reaction between PTZ and DDQ was also investigated. It seems reasonable to assume that anion radicals are formed from electron donor–acceptor interaction via a CT complex, as depicted in Eqs. (4) and (5). An increase in the polarity of the solvent would tend to stabilize the radical ion state, with respect to other states of the system, due to the ion–solvent interaction. It is possible that

Table V Kinetic and Thermodynamic Parameters for the Reaction of DDQ with PTZ

Solvent	ε_r	λ (nm)	$10^4\ k_1$ (s^{-1})			$\Delta H^{\#}$ (kJ mol^{-1})	$-\Delta S^{\#}$ (J K^{-1} mol^{-1})	$\Delta G^{\#}$ (kJ mol^{-1})
			298 K	305 K	313 K			
tert-Butyl alcohol	12.47	400	2.30	3.00	4.54	31.7	208	93.8
iso-Butyl alcohol	16.56	405	2.51	4.81	5.10	33.8	199	93.3
iso-Propanol	17.93	385	2.57	3.57	8.57	59.7	112	92.9
Acetone	20.70	425	2.78	3.29	8.27	54.3	132	93.6
DMF	36.50	364	10.8	17.8	24.9	40.4	166	89.9

ε_r, Relative permittivity of the medium.

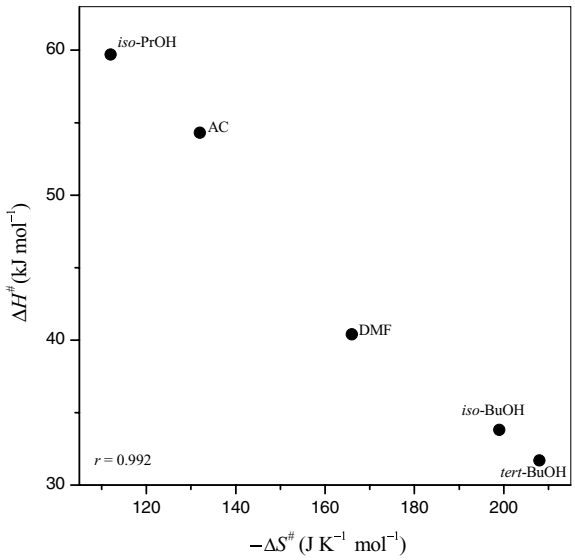


Figure 9 Relation between enthalpy and entropy of activations for the interaction of PTZ with DDQ.

the solvent interaction could also influence the first step (Eq. (4)), perhaps accompanied by an alteration of charge in the complex. Hereto, an increase in the polarity of the solvent could enhance the contribution of dative state and hence lead to a stronger charge transfer [46]. The results in Table V indicated that the k_1 values increased with an increase in the relative permittivity of the medium. This may be due to the fact that there is some charge separation in the transformation of CT complex to the final product. The involvement of such a polar transition state is well supported by the large negative entropies of activation in addition to the foregoing spectral studies. The negative entropy of activation also indicated a greater degree of ordering in the transition state than in the initial state, due to an increase in solvation during the activation process [22]. The positive enthalpy of activation values indicated that the reaction is endothermic in nature. The correlation between $\Delta H^{\#}$ and $\Delta S^{\#}$ values was found to be linear (Fig. 9; $r = 0.992$), indicating the operation of a common mechanism in the solvents investigated. In

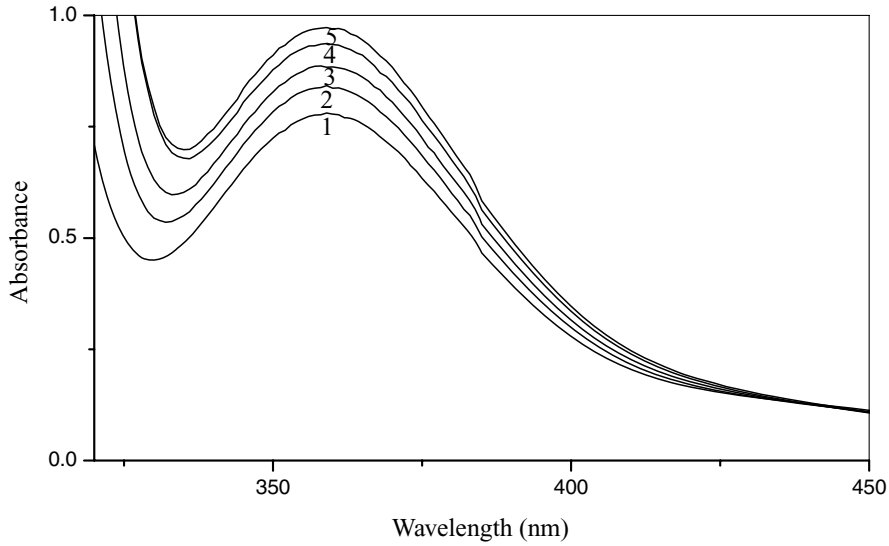
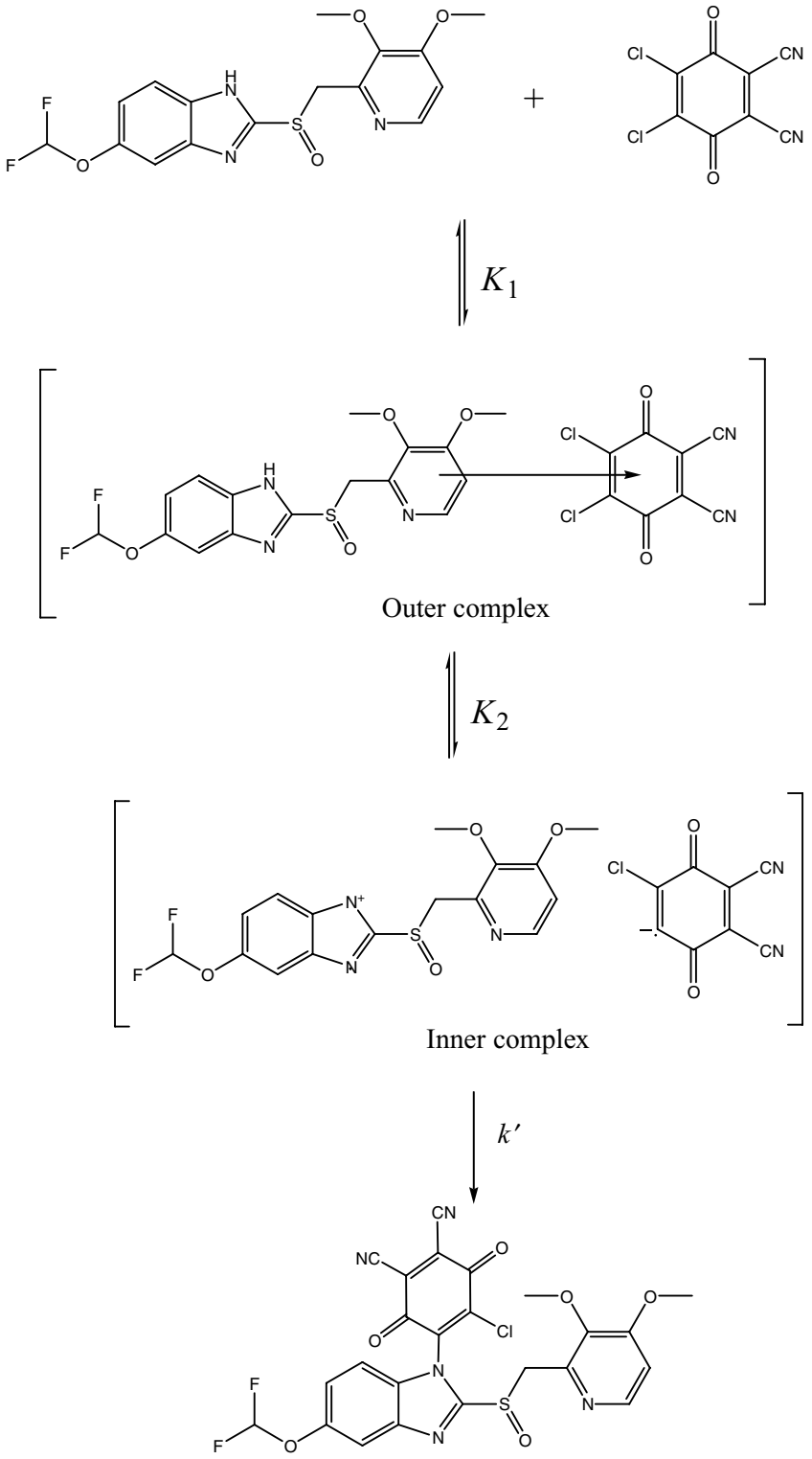


Figure 10 Electronic absorption spectra of PTZ—I_2 solution in *tert*-butyl alcohol at 298 K, showing the growth of the CT band at 358 nm. The iodine concentration is fixed at 9.1932×10^{-5} M, and the donor concentrations are 1, 1.72×10^{-4} M; 2, 3.45×10^{-4} M; 3, 5.17×10^{-4} M; 4, 6.89×10^{-4} M; and 5, 8.62×10^{-4} M.

this case also the plot of log k_1 versus ε_r (Fig. 4) showed a marked deviation from linearity especially at higher relative permittivity values, which indicated that the solvent–solvent interaction becomes increasingly significant, with an increase in the polarity of the medium, in addition to solute–solvent interactions. The solvent change from *tert*-butyl alcohol to DMF caused 24-fold rate acceleration for the reaction, which corresponds to a decrease in $\Delta G^{\#}$ of 4 kJ mol^{-1}.

Based on the foregoing results and discussions, the following plausible mechanism for the reaction of DDQ with PTZ has been proposed:



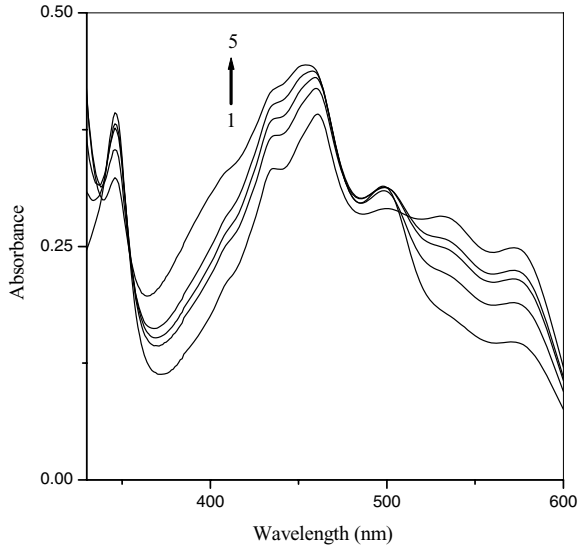


Figure 11 Electronic absorption spectra of PTZ–DDQ solution in *tert*-butyl alcohol at 298 K, showing the growth of the CT band at 433 nm. The DDQ concentration is fixed at 9.1773×10^{-5} M, and the donor concentrations are 1, 1.73×10^{-4} M; 2, 3.45×10^{-4} M; 3, 5.17×10^{-4} M; 4, 6.89×10^{-4} M; and 5, 8.61×10^{-4} M.

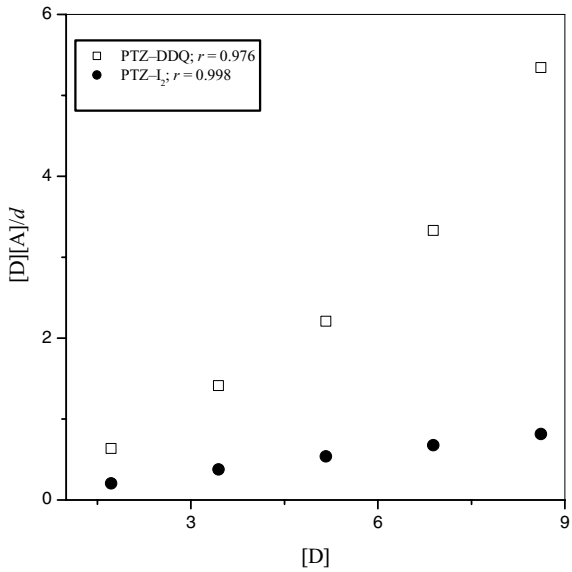


Figure 12 Scott linear plots for PTZ with DDQ and iodine at 298 K.

The above mechanism leads to the following rate law:

$$\mathrm{d[Product]}/\mathrm{d}t = k' \text{ [Inner complex]}$$

$$\text{or } \mathrm{d[Product]}/\mathrm{d}t = k \text{ [DDQ] [PTZ]}$$

where $k = k' K_1 K_2$.

The above rate law is in agreement with the observed kinetic results, i.e., the rate of reaction is first order each with respect to [DDQ] and [PTZ].

Characteristics of the CT Complexes

In both PTZ–I_2 and PTZ–DDQ systems, as enumerated earlier, initial reactants were converted in to final products via the formation of CT complexes. Hence, an attempt was made to characterize the CT complexes formed in these reactions. For that the absorbance of the new bands was measured using constant [A] (in a given solvent) and varying [D] depending on the solvent, but always [D] $\gg$ [A]. The variations in the electronic spectra with a change in [D] are shown in Figs. 10 and 11. The formation constants (K) and molar extinction coefficients (ε) of the CT complexes were determined spectrophotometrically using the Scott equation [47]

$$\frac{[\mathrm{D}][\mathrm{A}]}{d} = \frac{[\mathrm{D}]}{\varepsilon} + \frac{1}{K\varepsilon} \qquad (6)$$

where [D] and [A] are the initial molar concentrations of the donor and acceptor, respectively, and d is the absorbance. The values of K and ε are determined from the gradient and intercept of the linear plot of [D][A]/d against [D]. A representative Scott plot is shown in Fig. 12, and the values of K and ε determined are given in Table VI. In both the cases, the observed high values of K suggested that the formed CT complexes are of a strong type [48] and the linearity of the Scott plots further supports this result.

The values of oscillator strength (f), which is a measure of integrated intensity of the CT band and transition dipole moment (μ), were calculated as described elsewhere [49], and the values thus obtained are also given in Table VI. The values of f are rather relatively large, indicating a strong interaction between the donor–acceptor pairs with relative high probabilities of CT transitions [50]. Out of the many applications of CT complexes, one important application is to calculate the ionization potential of the donor. The ionization potential (Ip) of the highest filled molecular orbital of the donor was estimated from CT energies of its complexes with the acceptor making use of the empirical equations reported by Aloisi and Pingnataro [51].

$$\mathrm{Ip\,(eV)} = 5.76 + 1.52 \times 10^{-4}\ \bar{\nu}_{\mathrm{DDQ}}\ (\mathrm{cm}^{-1}) \qquad (7)$$

$$\mathrm{Ip\,(eV)} = 2.90 + 1.89 \times 10^{-4}\ \bar{\nu}_{\mathrm{Iodine}}\ (\mathrm{cm}^{-1}) \qquad (8)$$

The calculated Ip value for the molecular orbital participating in the CT interaction of the drug is shown in

Table VI Spectral Properties of the CT Complex Formed between the PTZ–DDQ and Iodine in *tert*-Butyl Alcohol Solvent at 298 K

Property	DDQ	Iodine
λ_{max} (nm)	572	358
$h\nu_{CT}$ (eV)	2.17	3.47
10^{14} ν_{max} (s^{-1})	5.24	8.38
Formation constant, K (dm^3 mol^{-1})	8075	13,584
Extinction coefficient, ε (dm^3 mol^{-1} cm^{-1})	1521	11,321
Oscillator strength, f	0.0124	0.2312
Dipole moment, μ	1.23	4.19
Ionization potential (eV)	8.42	8.18
Dissociation energy (eV)	4.34	1.64

Table VI. The ionization potential values calculated from the energies of the CT complexes formed with both the acceptors are in fairly good agreement with each other. Further evidence for the nature of CT interaction in the present systems is the calculation of the dissociation energy (W) of the CT excited state of the complex. The dissociation energies of the complex were calculated as described earlier [52], and the calculated values of W (Table VI) suggest that the investigated complex is reasonably strong and stable under the studied conditions with higher resonance stabilization energy [48].

CONCLUSIONS

Spectrokinetic studies revealed that the interaction of iodine and DDQ with PTZ drug was found to be proceed through three steps; out of these, the formation of outer complex and its conversion to inner complex are extremely fast, whereas the formation of the final product is the rate-determining slow step. The spectral, kinetic, and thermodynamic results support the proposed mechanism. The rate of the reaction was observed to increase with an increase in the relative permittivity of the medium. The results revealed that at higher relative permittivity regions solvent–solvent interaction is also significant in addition to solute–solvent interactions. The PTZ–I_2 system was characterized by the formation of tri-iodide ion, whereas the PTZ–DDQ system was characterized by the formation of the $DDQ^{-\bullet}$ radical ion. Both the acceptors form a 1:1 CT complex with the donor, and these complexes were found to be strong as evidenced from its equilibrium and spectral parameters. The mechanisms of the interaction of the drug studied may be useful in understanding the binding of the drug molecule in real pharmacokinetic study.

It is interesting to compare the results of the present study with those reported in the literature, particularly on the study of CT complexes of various drugs with these two acceptors. Parallel to the observations of the present study, drugs such as povidone and ketoconazole [22], dextromethorphan, and atenolol [23] interact with DDQ to form final products via the formation of quinone radical anion, which exhibited characteristic electronic spectral patterns. Likewise povidone and ketoconazole [24], dextromethorphan [23] and atenolol [53] interact with iodine, leading to the formation of a tri-iodide ion and which was confirmed by far-IR or Raman spectroscopy.

APPENDIX: CALCULATION OF RATE CONSTANTS

The pseudo-first-order rate constants (k_1) were calculated from the gradients of log (A_∞–A_t) against time plots, where A_∞ and A_t represent the absorbance at infinity and time t, respectively. The rate constant k_1 was calculated from the slope of the curve obtained from the linear plots of log (A_∞–A_t) against time, i.e.,

$$k_1 = \text{slope} \times 2.303$$

The second-order rate constants (k_2) were calculated by dividing k_1 by the donor concentration [D], i.e.,

$$k_2 = \frac{k_1}{[\mathrm{D}]}$$

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