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Spectroscopic studies on the interaction of cilostazole with iodine and 2,3-dichloro-5,6-dicyanobenzoquinone

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ABSTRACT

The electron accepting properties of the 2,3-dichloro-5,6-dicyanobenzoquinone and iodine and electron donating properties of the drug cilostazole have been studied using the UV–vis, FT-IR, GC–MS and Far-IR techniques. The interaction of cilostazole drug with iodine and 2,3-dichloro-5,6-dicyanobenzoquinone resulted via the initial formation of charge-transfer complex as an intermediate. The rate of formation of the product have been measured and discussed as a function of solvent and temperature. The complexes have been found by Job's method of continuous variation revealed that the stoichiometry of the complexes in both the cases was 1:1. The enthalpies and entropies of formation of the complexes have been obtained by determining their rate constant at three different temperature. The ionization potential of the donor was determined using the charge-transfer absorption bands of the complexes and the same was found comparable with that computed using MOPAC PM3 method.

1. Introduction

Over the years scientists have paid much attention on the spectral studies of charge-transfer (CT) complexes of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) and iodine with variety of donors [1–12]. Quinones are biologically significant molecules and are common constituent of many biologically relevant molecules. The reversible oxidation–reduction reactions of quinones play a key role in several biological processes [13,14]. Further, quinones are one of the well-known electron acceptors and the studies of their CT-interaction stem from their possible role in biological reactions [15,16]. Likewise iodine is also a biologically significant molecule [17–19]. Thus, the mechanism of interaction of these biologically important acceptors with drugs, in general, is a research topic of significant interest and hence the present study.

Chemically cilostazole is 6-(4-(1-cyclohexyl-1H-tetrazol-5-yl)butoxy)-3,4-dihydroquinolin-2(1H)-one. It is used to reduce the symptoms of intermittent claudication and helps people walk a longer distance. Hence, in continuation of our earlier works on the spectroscopic studies on the interaction of drug molecules with these acceptors [20–23], the present work report the CT interaction of cilostazole (CLZ) with DDQ and iodine. The spectral, kinetic and thermodynamic characteristics of the interaction between the donor drug and the acceptors were investigated and discussed.

2. Experimental

2.1. Material and methodology

The electron acceptors DDQ (minimum assay 98%) and iodine (minimum assay 99.9%) were obtained from Aldrich, India. Commercially available spectroscopy grade chloroform, dichloromethane, 1,2-dichloroethane, *tert*-butyl alcohol, *iso*-butyl alcohol, *iso*-propyl alcohol, methanol, acetonitrile and DMSO (all Merck, India, minimum assay > 99%) 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 CLZ was obtained as gift sample from a locally available pharmaceutical company and was used after confirming the purity. The purity of CLZ was checked by its m.p. (experimental 157–158 °C; theoretical 157–160 °C) and also by comparing its FT-IR spectrum with that of the authentic sample. The structure of the donor is shown below (Scheme 1).

Solutions for the spectroscopic measurements were prepared by dissolving accurately weighed amounts of donor (D) and acceptor (A) in the appropriate volume of solvent just before running the spectra. The electronic absorption spectra were 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 (±0.2 °C). The FT-IR spectra were recorded in a JASCO FT-IR 460 Plus spectrometer. The GC–MS spectra of the reaction product were obtained from Central Salt and Marine Research Institute, Bhavanagar, India. The molecular orbital package, MOPAC 2000 version 1.11 (PM3 method) was used for the

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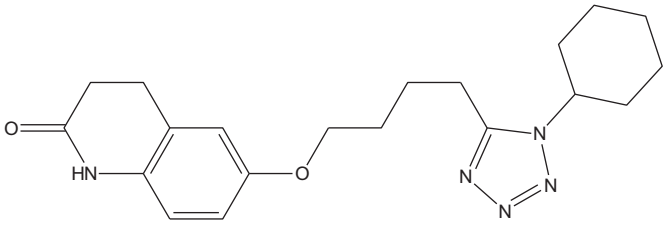


Scheme 1. Chemical structure of cilostazole.

theoretical calculation of the ionization potential of the donor [24]. The conductance of the solutions was measured on an Elico, India Conductivity Bridge. For 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.

2.2. Kinetic procedure

In both CLZ–I_2 and CLZ–DDQ cases, the kinetics of the interaction was followed under pseudo-first-order conditions at three different temperatures in various solvents, keeping [D] ≫ [A]. The increase in absorbance of the product around 350 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 were calculated by dividing k_1 by [D].

3. Results and discussion

3.1. Stoichiometry of the reaction

The stoichiometry of the CT-complex, in both the cases, was determined by applying Job's continuous variation method [25]. The absorbances of several solutions, so as to have [D] + [A] = constant, but with varying D:A ratio, are measured at 360 nm in methanol for the iodine complex and at 348 nm in acetonitrile for the DDQ complex. The total concentrations of the donor and acceptor are 9.02×10^{-4} M and 11.55×10^{-4} M in iodine and DDQ systems, respectively. The symmetrical curves with maximum at 0.5 mole fraction indicated the formation of a 1:1 (D:A) CT-complex (Fig. 1). The photometric titration measurements were also performed for the determination of the stoichiometry in these interactions. For that, the concentration of the donor in the reaction mixtures was kept fixed while those of the acceptors were varied over a wide range. In the case of iodine complex, the measurements were carried out at 360 nm in methanol at a donor concentration of 2.15×10^{-4} M with acceptor concentration in the range of 5.42×10^{-5} to 2.17×10^{-4} M. In the case of DDQ complex, the measurements were carried out at 334 nm in *tert*-butyl alcohol at a donor concentration of 3.68×10^{-4} M with acceptor concentration ranging from 9.25×10^{-5} to 3.70×10^{-4} M. The results of the photometric curves (Fig. 2) also indicated that the stoichiometry of the interaction, in both the cases, is 1:1 (D:A) [26].

3.2. Characterization of the reaction products

In both CLZ–I_2 and CLZ–DDQ cases, the reaction product was obtained by allowing the reactants to react for 24 h under equal molar conditions in a given solvent and subjected to MPLC (Medium Pressure Liquid Chromatographic (Buchi, Switzerland)) separation. The FT-IR spectra of the products were recorded and the peak

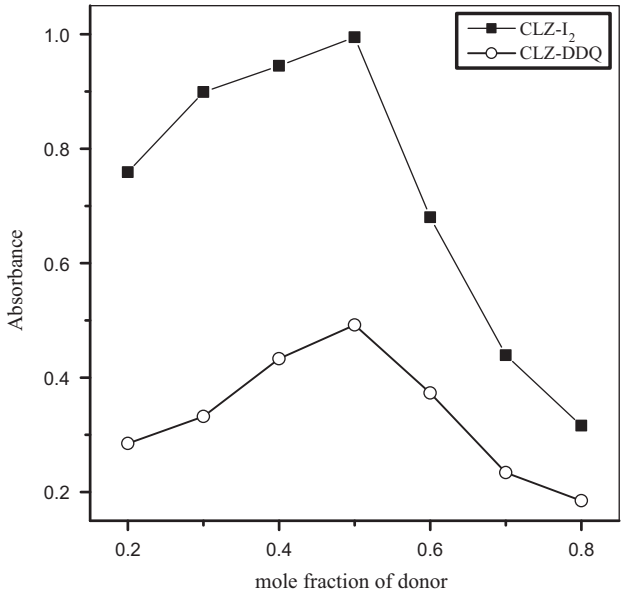


Fig. 1. Job's continuous variation method for CLZ–I_2 in methanol and CLZ–DDQ in acetonitrile at 298 K.

assignments for important peaks are given in Table 1. 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 donor and acceptor 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 CLZ occurs at 3322 cm^{-1} and in DDQ and iodine complexes they appear at 3316 and 3315 cm^{-1} respectively. The ν(C=O) and ν(C–Cl) stretching vibrations in the DDQ species appeared at 1679 and 799 cm^{-1} respectively. In the product these stretching vibrations occurred at 1670 and 707 cm^{-1}, respectively. Such a bathochromic shift could be indicative of a higher charge density on the carbonyl and C–Cl groups of the DDQ molecule [20,21]. As there are no significant changes in the FT-IR spectrum of the CLZ–I_2 complex when compared to that of the constituents, we have recorded Far-IR spectrum to explain the complex formation. The far infrared spectrum of the

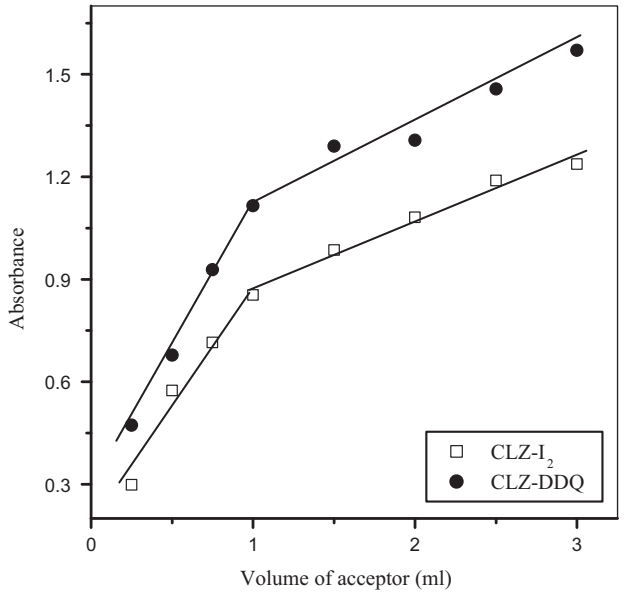


Fig. 2. Photometric titration plots of CLZ with iodine in methanol and CLZ with DDQ in tert-butyl alcohol at 298 K.

Table 1
Infrared wave number (cm^{-1}) and tentative band assignments for the drug (CLZ), and its complex with iodine and DDQ.

CLZ	DDQ	CLZ–DDQ	CLZ–I_2	Assignments
3430b		3433b	3432b	ν(–OH) stretching
3322m		3316m	3315m	ν(N–H); stretching
3183m		3182m	3187m	
3112w		3105w	3111w	
2934m		2934m	2928m	ν(C–H); aliphatic
	2226m			ν(C≡N)
	2203s			
		2228w		ν(C≡N)
	1679m			ν(C=O)
				ν(C=C)
1669s		1670s	1660s	ν(C=O)
1595w		1591w	1592w	ν(C=C); aromatic
1505s		1505s	1505s	δ(N–H); bending
1478w		1474w	1471w	$\delta(CH_2)$; bending
1455w		1455w	1453w	
1399m		1399m	1396m	δ(C–H); bending
1269w		1274w	–	ν(C–N); aromatic
1243s		1243s	1243s	ν(C–O); aromatic ether
1197w		1196w	1195w	ν(C–C); aliphatic
1038m		1038m	1038m	ν(C–O); aliphatic ether
	799s			ν(C–Cl)
	771w			
		707w	–	ν(C–Cl)
		673m	–	

s, strong; m, medium; w, weak; br, broad; ν, stretching; δ, bending.

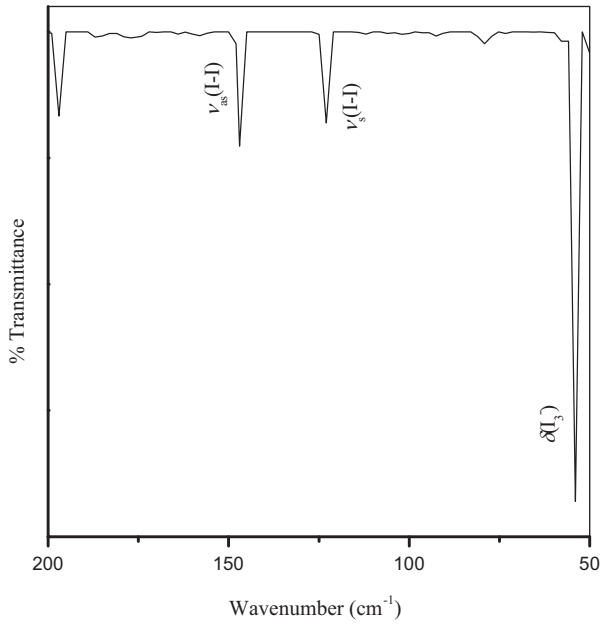
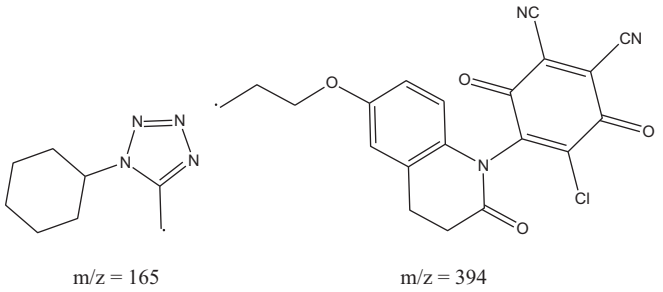


Fig. 3. Far-IR spectra of $[(CLZI)]^+I_3^-$ complex.

CLZ–I_2 complex is shown in Fig. 3 and the spectral data are collected in Table 2. The spectrum showed the characteristic bands of I_3^- ion at 147, 123 and 54 cm^{-1}. It is well known that I_3^- ion exists as one unit with either linear or bent structures [27,28]. The group theoretical analysis showed that the three vibrations should be infrared active. The 147 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 123 cm^{-1}. The band at 54 cm^{-1} is assigned to the bending vibration, $\delta(I_3^-)$ [29,30]. These assignments are exactly similar to those known for the non-linear I_3^- ion. The results in the present study, therefore, indicated the presence of non-linear triiodide ion in the CLZ–I_2 complex. Based on the foregoing results the formula of the formed complex is $[(CLZ)\,I]^+\,I_3^-$.

Table 2
Fundamental Far-IR vibrations for I_3^- ion.

Compound	Assignments			Reference
	ν_{as}(I–I)	ν_s(I–I)	$\delta(I_3^-)$	
CsI_3	149	103	69	[27]
$[(DAPY)I]\,I_3^-$	151	132	61	[28]
$[Fe(acac)_3]_2\,I^+\,I_3^-$	150	102	76	[30]
$[(HMTACTD)I]\,I_3^-$	144	110	60	[29]
$[(CLZ)I]^+\,I_3^-$	147	123	54	Present work



Scheme 2.

Product analysis, in the case of CLZ–DDQ system, was carried out by employing GC–MS technique. The mass spectrum of the product displayed the following major peaks at the given corresponding *m*/*z* values confirms the structure of the reaction product (Scheme 2).

In the case of CLZ–I_2 complex thermal analysis (TG) was also carried out to a certain the proposed formula. The TGA curve (Fig. 4) indicated that the complex undergoes decomposition in the temperature range 296–694 °C with a weight loss of 97.1%. The DSC curve with a maximum at 365 °C indicated that the compound undergoes decomposition in a single step, exothermically. Parallel observation was made by us in the study of charge transfer complex of atenolol with iodine [31].

3.3. Interaction of cilostazole with iodine

The solutions of cilostazole and iodine in *iso*-butyl alcohol are mixed; there was an instantaneous formation of lemon yellow color with new absorption maxima at 360 nm in the UV–vis spectrum (Fig. 5), which is the blue-shifted iodine band. 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 donor [32,33]. 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 donor and iodine molecules. The limiting value of this shift is at 360 nm, which is the characteristic absorption of the I_3^- ion in solution. Parallel observations were made by us [28,34] and also by several investigators in the study of molecular complexes of iodine with variety of donor molecules [9,35].

It is observed that the intensity of the band at 460 nm decreased while the intensity of the characteristic I_3^- ion band at 360 nm increased with elapse of time. A clear isosbestic point was observed at 445 nm. Consequently, the change in absorbance of the solution, at 360 nm, was measured as a function of time. No attempt was made to measure the decrease in intensity of the peak at 460 nm, as the peak reach a constant value quickly in majority of the solvents. And also the increase in intensity of the peak at around 290 nm as the intensity is very high.

The observed time dependent electronic spectrum of the system under investigation is due to a transformation of the initially

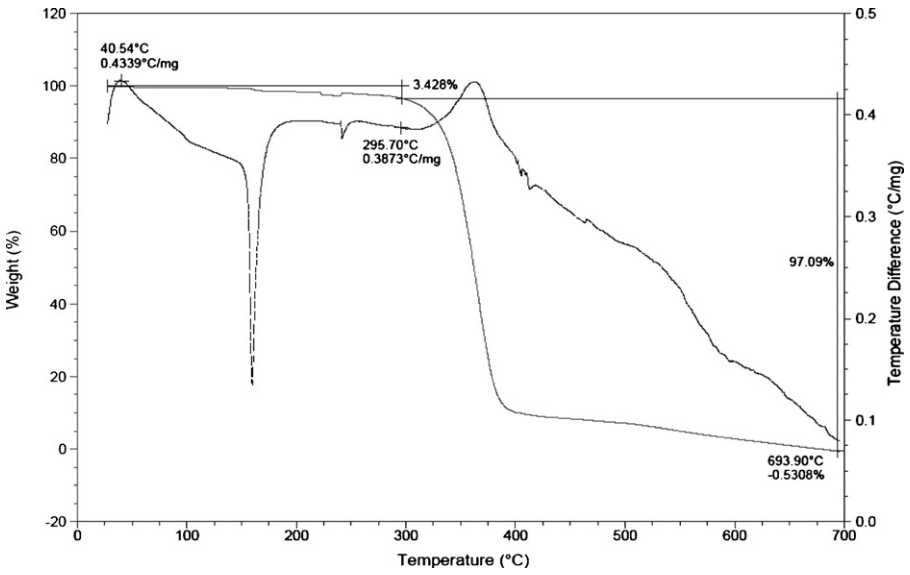


Fig. 4. TGA and DSC curves for $[(CLZ)\,I]^{+}\,I_3^{-}$ complex.

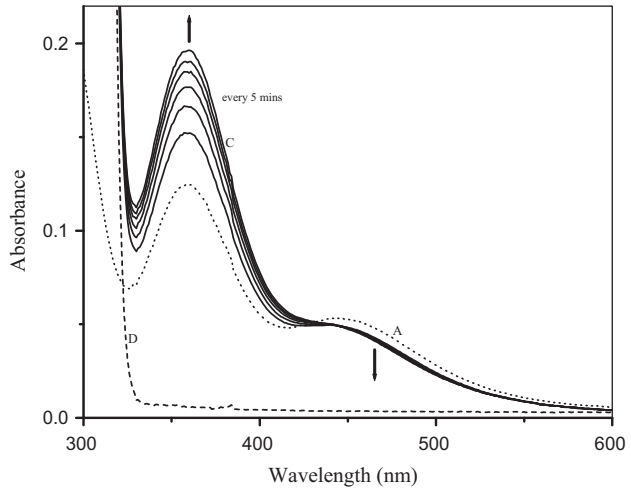


Fig. 5. Electronic absorbance spectrum of CLZ with iodine in iso-butyl alcohol at 298 K with elapse of time.

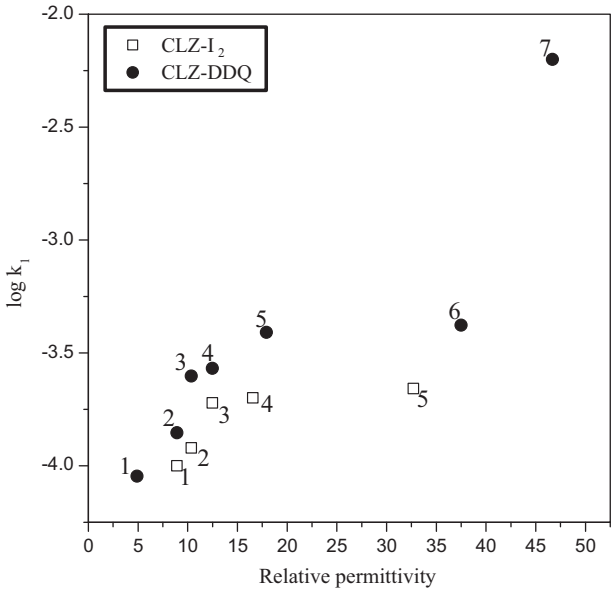


Fig. 6. Plot of $\log k_1$ vs. relative permittivity of the medium.

formed outer complex (CT complex) into an inner complex followed by a fast reaction of the resulting inner complex with iodine to form a triiodide ion, as depicted below [9,22,35,36].

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

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

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

The rate constants as a function of temperature and solvent along with thermodynamic parameters for the CLZ–I_2 reaction are collected in Table 3. The k_1 values were found to increase with an increase in the relative permittivity of the medium. There is a deviation from linearity in the plot of $\log k_1$ versus relative permittivity of the medium (ε_r) especially at higher ε_r values (Fig. 6). This may be due to the fact that with increase in polarity of the medium

Table 3
Kinetic and thermodynamic parameters for the reaction of iodine with cilostazole.

Solvent	ε_r[a]	λ (nm)	$10^4 k_1$ (s^{-1})			$\Delta H^{\neq}$	$-\Delta S^{\neq}$	$\Delta G^{\neq}$
			298 K	305 K	313 K			
Dichloromethane	8.93	364	1.0	1.4	1.5	21	252	95.8
1,2-Dichloroethane	10.36	363	1.2	1.8	7.2	93	8	95.9
tert-Butyl alcohol	12.47	361	1.9	2.4	7.1	65	99	94.5
iso-Butyl alcohol	16.56	360	2.0	2.7	4.1	35	200	94.1
Methanol	32.70	360	2.2	2.8	4.4	34	201	94.0

[a] Relative permittivity of the medium from Ref. [50]; $\Delta H^{\neq}$, kJ mol^{-1}; $\Delta S^{\neq}$, J K^{-1} mol^{-1}; $\Delta G^{\neq}$, kJ mol^{-1}.

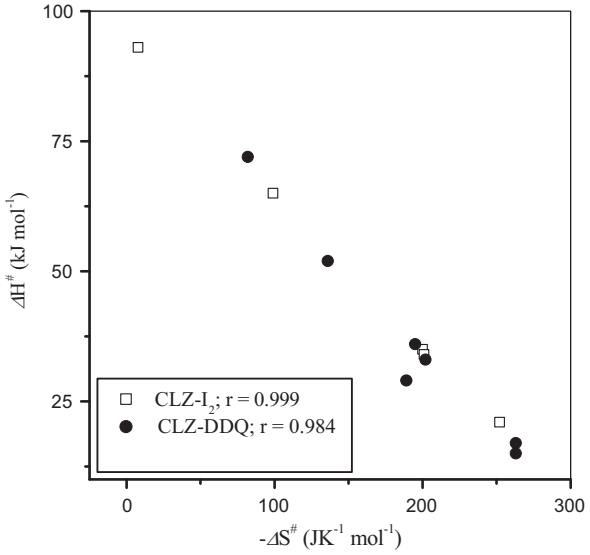


Fig. 7. Relation between enthalpy and entropy of activations for the interaction of CLZ with DDQ and iodine in different solvents.

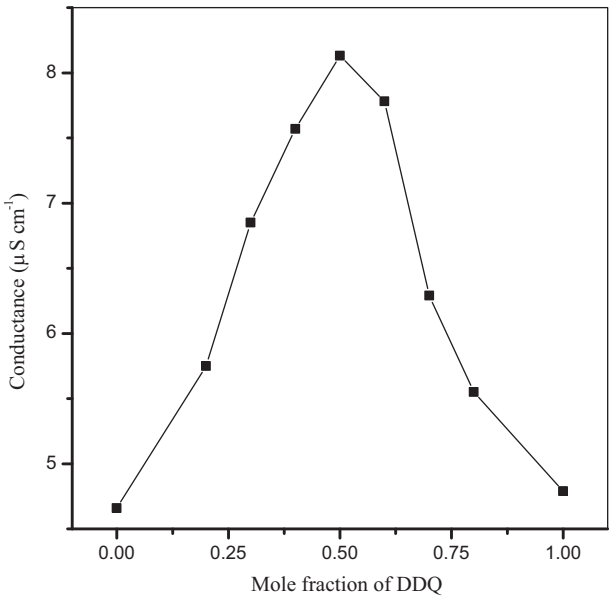


Fig. 8. Conductivity vs. volume of DDQ plot for CLZ–DDQ system in acetonitrile at 298 K.

solvent–solvent interaction becomes increasingly significant in addition to solute–solvent interactions. This solvent dependence of 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 entropies of activation observed [20]. Further, negative entropy of activation 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. There exists linear correlation between $\Delta H^{\neq}$ and $\Delta S^{\neq}$ values (Fig. 7, $r = 0.999$) indicating the operation of a common mechanism in all the solvents studied. A perusal of data in Table 3 indicated that a solvent change from dichloromethane to methanol caused ~2-fold rate acceleration for the reaction which corresponds to a decrease in $\Delta G^{\neq}$ of 2 kJ mol^{-1} at 298 K.

3.4. Interaction of cilostazole with DDQ

Conductimetry has often been employed to study the interactions of CT complexes [37–39]. In the present study, a mixture of acetonitrile solutions of CLZ and DDQ exhibited appreciable conductivities which may be due to the formation of a CT-complex. The conductivity-mole fraction of DDQ plot, shown in Fig. 8, yielded maximum at a D:A molar ratio of 1:1. 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 as shown below [20,40].

$$D + A \rightleftarrows DA \quad (4)$$

$$DA \rightleftarrows [D^{+}A^{-}] \quad (5)$$

The electronic absorption spectra of DDQ in the presence of a large excess of the donor, i.e. [D] ≫ [A] was obtained as a function of time in different solvents. The electronic absorption spectra of the mixture of methanolic solutions of CLZ and DDQ show a group of absorption bands at 430, 452, 548 and 590 nm (Fig. 9). These absorption bands are characteristic for the absorption of the radical anion $DDQ^{\bullet -}$ [4,17,22,41,42]. The observed enhanced absorption band intensities, immediately after mixing D and A, supports the fact that the CT complex formed is of dative-type structure which consequently converts to an ionic intermediate possessing the spectral characteristics of radical ion [20,21]. Further, the observed gradual decrease in the intensity of the CT bands in the 400–600 nm spectral regions with elapse of time could be due to the consumption of the ionic intermediate through an irreversible chemical reaction, while the continuous increase of the 350 nm band with elapse of time is indicative of the formation of the final reaction product [39]. A clear isosbestic point at 360 nm was also observed.

The effect of solvent on the reaction between the CLZ 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). Increase in polarity of the solvent would tend to stabilize the radical ion state, with respect to other states of the system, due to ion–solvent interac-

Table 4
Kinetic and thermodynamic parameters for the reaction of DDQ with cilostazole.

Solvent	ε_r[a]	λ (nm)	$10^4 k_1$ (s^{-1})			$\Delta H^{\neq}$	$-\Delta S^{\neq}$	$\Delta G^{\neq}$
			298 K	305 K	313 K			
Chloroform	4.90	351	1.0	1.9	4.0	72	82	95.9
Dichloromethane	8.93	350	1.4	1.5	2.0	17	263	95.9
1,2-Dichloroethane	10.36	354	2.5	2.6	3.5	15	263	93.7
tert-Butyl alcohol	12.47	334	2.7	3.2	5.6	36	195	93.5
iso-Propyl alcohol	17.93	352	3.9	6.4	7.7	33	202	92.3
Acetonitrile	37.50	348	4.2	6.1	12	52	136	92.4
DMSO	46.68	354	63	76	116	29	189	86.0

[a] Relative permittivity of the medium from Ref. [50]; $\Delta H^{\neq}$, kJ mol^{-1}; $\Delta S^{\neq}$, J K^{-1} mol^{-1}; $\Delta G^{\neq}$, kJ mol^{-1}.

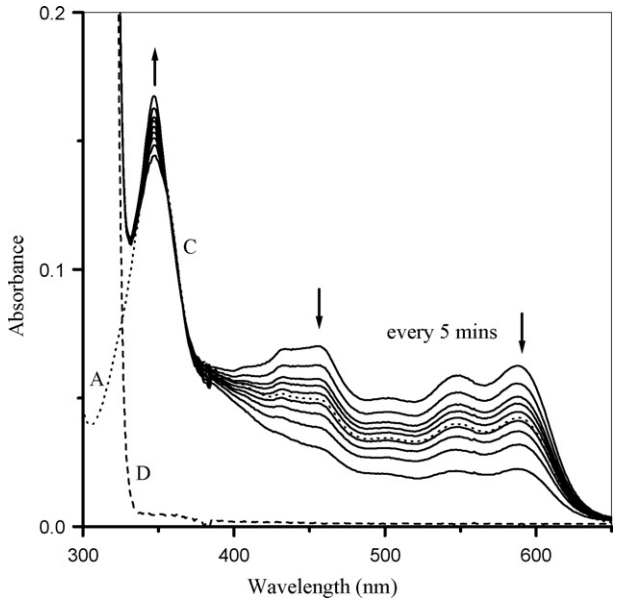


Fig. 9. Electronic absorbance spectrum of CLZ with DDQ in acetonitrile at 298 K as a function of time.

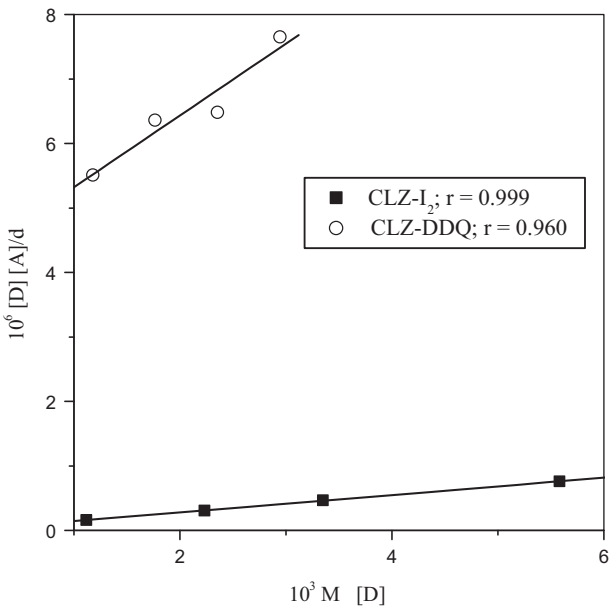


Fig. 10. Scott linear plots for CLZ–iodine in methanol and CLZ–DDQ in acetonitrile at 298 K.

tion. It is possible that the solvent interaction could also influence the first step (Eq. (4)), perhaps accompanied by an alteration of charge in the complex. Hereto, increase in polarity of the solvent could enhance the contribution of dative state and hence lead to a stronger charge transfer [43]. The results in Table 4 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. Involvement of such a polar transition state is well supported by the large negative entropies of activation. 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 [21]. A plot of $\log k_1$ versus relative permittivity of the medium (Fig. 6) showed a deviation from linearity at higher ε_r values indicating an enhanced solvent–solvent interaction in these media. The correlation between $\Delta H^{\neq}$ and $\Delta S^{\neq}$ values was found to be linear (Fig. 7, $r = 0.984$) indicating the operation of a common mechanism in the solvents investigated. The solvent change from chloroform to DMSO caused ~63-fold rate acceleration for the reaction which corresponds to a decrease in $\Delta G^{\neq}$ of 10 kJ mol^{-1}.

Based on the foregoing results and discussions the following plausible mechanism for the interaction DDQ with cilostazole has been proposed. The final product formed in the interaction has been confirmed using GC–MS technique. The mass spectrum of the product yielded a peak at m/z vales 560 indicated the formation of the suggested product (Scheme 3).

The above mechanism leads to the following rate law.

$$\frac{d[\text{Product}]}{dt} = k[\text{Complex}]$$

$$\text{or} \quad \frac{d[\text{Product}]}{dt} = k'[\text{DDQ}][\text{CLZ}]$$

where $k' = kK$

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

Table 5
Spectral properties of the CT complexes formed between the cilostazole with iodine in methanol and DDQ in acetonitrile solvent at 298 K.

Property	DDQ	Iodine
λ_{max} (nm)	589	360
$h\nu_{CT}$ (eV)	2.11	3.46
$10^{14}\nu_{max}$ (s^{-1})	5.09	8.36
Formation constant, K (dm^3 mol^{-1})	261	13,092
Extinction coefficient, ε (dm^3 mol^{-1} cm^{-1})	909	7445
Oscillator strength, f	0.0005	0.1624
Dipole moment, μ	0.8253	3.52
Ionization potential (eV)	8.34 (8.55)[a]	8.16 (8.55)[a]
Dissociation energy (eV)	4.32	2.01

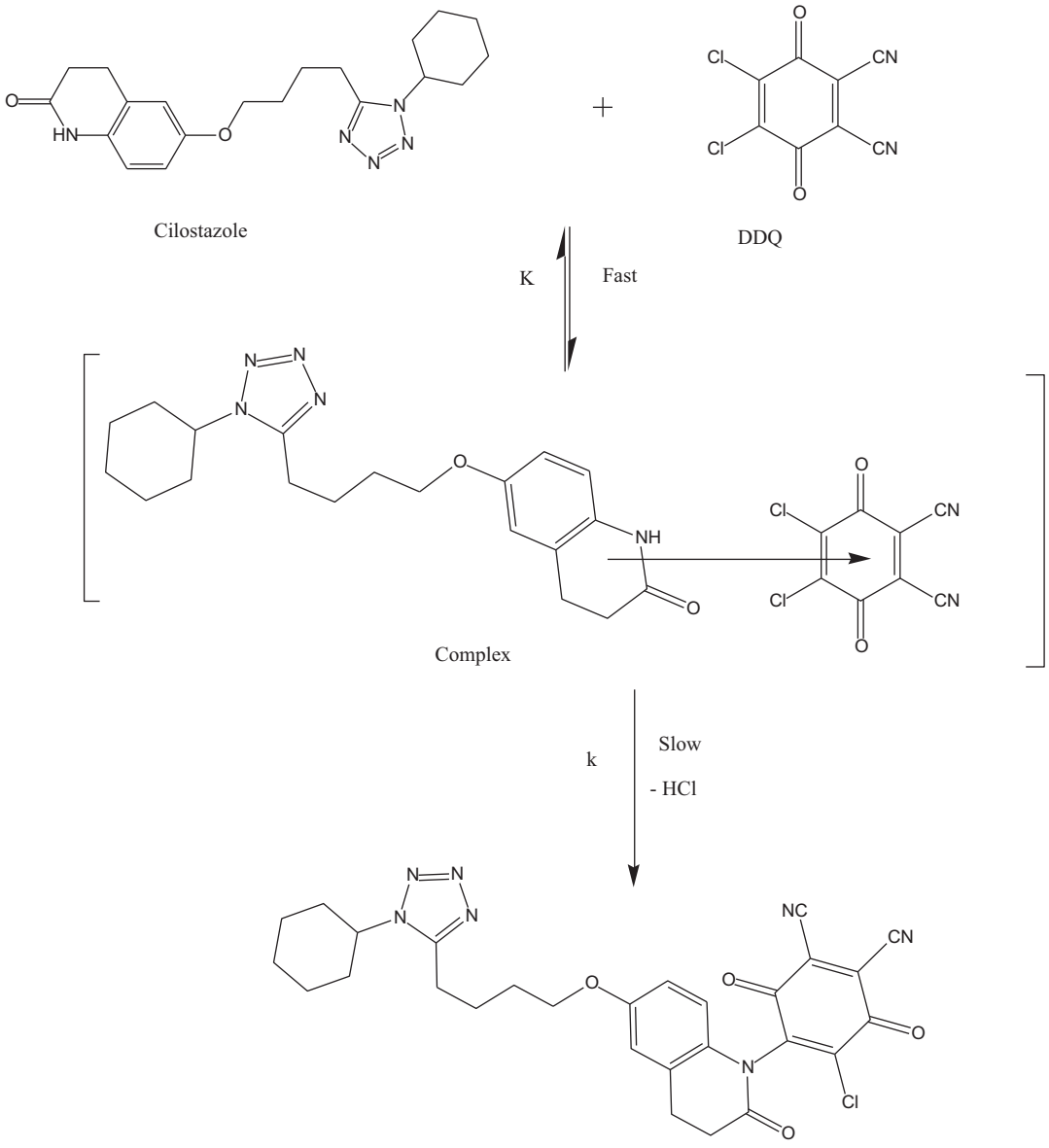
[a] Calculated by MOPAC (PM3) method.

3.5. Characteristics of the CT Complexes

In both CLZ–I_2 and CLZ–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 at 589 nm and 360 nm for CLZ–DDQ and CLZ–I_2 complexes, respectively, were measured using constant acceptor concentration (in a given solvent) and varying concentrations of the donor depending on the solvent, but always [D] ≫ [A]. The formation constants (K) and molar extinction coefficients (ε) of the CT-complexes were determined spectrophotometrically in the temperature range 298–313 K using the Scott equation [44]. For a 1:1 complex, this equation can be written as:

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

where [A] and [D] are the initial molar concentrations of the electron acceptor and the electron donor, respectively. ℓ is the optical path length of the cell and d is the absorbance of the complex. Eq. (6) is applicable when [D] ≫ [A] and the complex absorbs at a wavelength where both electron acceptors and donors are completely transparent. K and ε were calculated from the slope and the intercept of the curve obtained from the linear plots of $[A][D]\ell/d$ against [D]. A representative Scott plot is shown in Fig. 10 and the values of K and ε determined are given in Table 5. The observed high val-



Scheme 3.

ues of K suggested that the CT-complexes formed are of a strong type [45] and the linearity of the Scott plots further supported 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 [22] and the values thus obtained are also given in Table 5. The values of f are rather relatively large indicating a strong interaction between the donor–acceptor pairs with relative high probabilities of CT-transitions [46,47]. 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 in literature [48].

$$I\text{p}\ \ (\text{eV}) = 5.76 + 1.52 \times 10^{-4}\bar{\nu}_{\text{DDQ}}\ \ (\text{cm}^{-1}) \tag{7}$$

$$I\text{p}\ \ (\text{eV}) = 2.90 + 1.89 \times 10^{-4}\bar{\nu}_{\text{Iodine}}\ \ (\text{cm}^{-1}) \tag{8}$$

The calculated Ip value for molecular orbital participating in CT-interaction of the donor is listed in Table 5. In the present study, the theoretical (MOPAC PM3 method) and experimental ionization potential values are in fairly good agreement with each other. This fact supports the interpretation that the low energy band can be regarded as the CT band. Further evidence for the nature of CT-interaction in the present systems is the calculation of the dissociation energy (W) of the charge-transfer excited state of the complex. Hence the dissociation energies of the complex were calculated from their CT-energy, $h\nu_{\text{CT}}$, the ionization potential of the donor, Ip and electron affinity, E^{A}, of the acceptor using the empirical relation [20,49] given in Eq. (9):

$$h\nu_{\text{CT}} = I\text{p} - E^{\text{A}} - W \tag{9}$$

The calculated values of W (Table 5) suggested that the investigated complex is reasonably strong and stable under the studied conditions with higher resonance stabilization energy [45].

4. Conclusions

Spectro-kinetic studies revealed that the interaction of iodine and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone with CLZ 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 CLZ–I_2 system was characterized by the formation of triiodide ion while the CLZ–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.

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