Spectrochimica Acta Part A 79 (2011) 1621–1629

Contents lists available at ScienceDirect

Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy

journal homepage: www.elsevier.com/locate/saa

Spectroscopic and spectrofluorimetric studies on the interaction of irbesartan with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone and iodine

K. Ganesh, C. Balraj, K.P. Elango*

Department of Chemistry, Gandhigram Rural Institute (Deemed University), Gandhigram 624 302, India

ARTICLE INFO

Article history:
Received 28 August 2010
Received in revised form 21 April 2011
Accepted 16 May 2011

Keywords:
Charge transfer
Irbesartan
DDQ
Iodine
Fluorescence
Solvent effect

ABSTRACT

Raman, UV–vis, ^{1}H NMR, FT-IR, mass and fluorescence spectral techniques were employed to investigate the mechanism of interaction of irbesartan (IRB) drug with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and iodine. Interaction of IRB with iodine yields triiodide ion and its formation was confirmed by electronic and Raman spectra. The peaks appeared in Raman spectrum of the isolated product at 143, 113 and 76 cm^{-1} are assigned to ν_{as}(I–I), ν_s(I–I) and $\delta(I_3^-)$ respectively, confirmed the presence of I_3^- ion. The interaction of DDQ with irbesartan was found to proceed through the formation of outer complex and its conversion to the CT complex. Formation constant (K), molar extinction coefficient (ε) and thermodynamic properties $\Delta H^{\#}$, $\Delta S^{\#}$ and $\Delta G^{\#}$ were determined and discussed. Fluorescence quenching studies indicated that the interaction between the IRB and the acceptors are spontaneous and the IRB–DDQ interaction is found to be stronger than that the other system. Solvent variation studies indicated that the binding constant increased with an increase in polarity of the medium.

1. Introduction

Charge transfer (CT) phenomenon was introduced first by Mulliken [1,2] and discussed widely by Foster [3]. The CT complexes originated from interaction between electron donor and acceptor molecules in bimolecular equilibrium or in model compounds with intramolecular interaction have been an important topic of research in physical chemistry and biochemistry in last few decades [4–16]. Further CT interactions play an important role in biological process such as photosynthesis, oxidative processes in living cells, drug action, enzyme catalysis, ion transfer through lipophilic membranes and act as intermediates in a wide variety of reactions involving nucleophiles and electron deficient molecules [17,18]. Also the CT systems are being used in many area of material science such as in optochemical sensors in the design of optoelectronic devices, in doping of organic semiconducting polymers etc. [19–24].

Iodine is an essential element that enables the thyroid gland to produce thyroid hormones, which is the master gland of metabolism. The study of interaction of iodine as electron acceptor with various types of donors such as drugs, amines, polyamines etc. is of important and interesting area of research [16,25,26]. Likewise quinones are one of the well known important classes of electron acceptors. The studies of quinones for their CT interaction stem from their possible role in biological reactions [27]. Thus, the mechanism of interaction of iodine and a quinone with drugs, in general, is a research topic of significant interest and hence the present study. The objective, therefore, of the present article is to study the spectral, thermodynamic and kinetic aspects of the interaction of the electron acceptors DDQ and iodine with irbesartan (IRB) drug with an aim to investigate the mechanism of these interactions. In general, drugs are poly-functional organic molecules and the present study aims at to investigate the actual site of attack during the formation of charge transfer interactions. Such a study would undeniably shed some light on the mechanism of the drug action in real pharmacokinetic study. Irbesartan is a non peptide compound and is chemically known as 2-butyl-3-[*p*-(*o*-1H-tetrazol-5-ylphenyl)benzyl]-1,3-diazaspiro[4,4]non-1-en-4-one. It is an antagonist II receptor (AT_1) mainly used for the treatment of hypertension [28].

2. Experimental

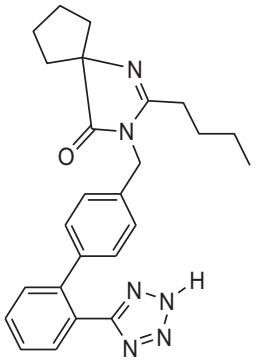
2.1. Materials and methodology

The electron acceptors DDQ (minimum assay 98%) and iodine (minimum assay 99.9%) were obtained from Aldrich, India and were used as received. Commercially available spectroscopic grade solvents (Merck, India) were used without further purification. The drug irbesartan was obtained as gift sample from locally available pharmaceutical company and was used as received. The purity of the drug was checked by its melting point (observed 180 °C and

* Corresponding author. Tel.: +91 451 245 2371; fax: +91 451 2454466.
E-mail address: drkpelango@rediffmail.com (K.P. Elango).

1386-1425/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.saa.2011.05.022

theoretical 180 °C), ^{1}H NMR and FT-IR spectra. The structure of the drug is shown below.



Chemical structure of Irbesartan

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 were recorded on a JASCO (V 630, Japan) 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 steady state fluorescence spectra were obtained on a JASCO (FP 6200, Japan) spectrofluorimeter. The excitation wavelength was 280 nm and the emission was monitored at 365 nm. The excitation, emission slit width (5 nm) and the scan rate (250 nm) was kept constant for all of the experiments. FT-IR spectra were recorded in a JASCO (FT-IR 460 Plus, Japan) spectrometer. ^{1}H NMR spectra were recorded at Madurai Kamaraj University, Madurai in a Brucker NMR spectrometer (300 MHz, Switzerland). The GC–MS spectra were obtained from Central Salt and Marine Research Institute, Bhavanagar, India. The laser Raman spectra were recorded at Indian Institute of Technology, Chennai in a Bruker (IFS 66V/FRA 106) FT Raman Spectrometer. Thermal studies (TGA/DSC) were carried out at the Central Electrochemical Research Institute, Karaikudi in a Perkin Elmer analyser (TGA 7 series, USA).

2.2. Kinetic procedure

In both IRB–I_2 and IRB–DDQ cases, the kinetics of the interaction was followed at three different temperatures in various solvents under pseudo-first-order condition, keeping [D]/[A] > 100 as described earlier [29]. The increase in absorbance of the new 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 were calculated by dividing k_1 by [D].

3. Results and discussion

3.1. Stoichiometry of the interaction

The stoichiometry of the CT complex, in both the cases, was determined by applying Job's continuous variation method [30]. The symmetrical curves with a maximum at 0.5 mole fraction indicated the formation of a 1:1 (D:A) CT complex (Supplemental information Fig. 1S). The photometric titration measurements were also performed for the determination of the stoichiometry in these interactions. The results of the photometric titration studies (figure not shown) also indicated that the stoichiometry of the interaction, in both the cases, is 1:1 (D:A) [31].

3.2. Characterization of the CT complexes

In both IRB–I_2 and IRB–DDQ cases, the CT complex was obtained by allowing the reactants to react for 24 h under equal molar conditions in a given solvent and subjected to MPLC separation. The FT-IR spectra of the products were recorded and the peak assignments for important peaks are given in (supplemental information Table S1). The results indicated that the shifts in positions of some of the peaks could be attributed to the symmetry and electronic structure modifications in both donor and acceptor units in the formed CT complex relative to the free molecules. Some of the significant shifts are: the peak due to ν(N–H) vibration of the free irbesartan occurred at 3444 cm^{-1} and in DDQ and iodine complexes it appeared at 3412 and 3434 cm^{-1}, respectively indicating the participation of the N–H moiety in the complexation process. 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 CT-complexes these stretching vibrations occurred at 1628, 2224 and 758 cm^{-1}, respectively. Such a bathochromic shift could be indicative of an increase in the polarity of the carbonyl and chloro groups of the DDQ molecule [15].

The ^{1}H NMR spectra of the donor and the IRB–DDQ complex were recorded in DMSO d^6 and are given in Fig. 1. Using the proton NMR technique, we can identify the nature of interaction between the donor and acceptor in the resulted complex. Pure IRB molecule exhibited the characteristic tetrazole N–H peak at 16.28 ppm. In the IRB–DDQ complex, it lies at 16.36 ppm indicating the involvement of the N–H group in the CT complex formation with the acceptor. Though the observed shift is very marginal, the result along with FT-IR results supports the conclusion. The aromatic protons of the donor which lie in the range of 7.08–7.70 ppm showed no significant variation in the complex indicating non participation of the aromatic rings in the CT complex formation. In the donor the CH moiety, which connects phenyl ring and nitrogen atom lies at 4.68 ppm and in the complex at 4.69 ppm [32,33]. The mass spectrum of the IRB–DDQ complex exhibited ionization peaks alone corresponding to the donor and acceptor individually instead of a peak for the combined one which revealed that there should be an interaction of CT type between the donor and acceptor molecule rather than a chemical reaction between them leading to a new chemical species.

As a representative case, the TGA–DSC analysis of the IRB–I_2 complex was carried out to ascertain the proposed formula. The TGA curve (Fig. 2) indicated that the complex undergoes decomposition in two stages. The first stage corresponds to the loss of triiodide ion in the temperature range 137–360 °C (DSC maximum at 232 °C) with a weight loss of 48.26% (cal. 40.66%) and the second stage corresponds to the loss of drug in the temperature range 360–590 °C (DSC maximum at 539 °C) with a weight loss of 50.14% (cal. 59.33%). The thermal analysis confirmed the proposed formula as $[(IRB)I]^+I_3^-$.

3.3. Interaction of irbesartan with iodine

On mixing *tert*-butyl alcoholic solutions of IRB and iodine, there was an instantaneous formation of lemon yellow colour with absorption maxima centered at 360 nm in the UV–vis spectrum (Fig. 3). The absorption band at 360 nm is the blue-shifted iodine band, which is characteristic of n-donor-iodine CT complex [34]. The absorption band around 482 nm, which is attributed to the $\pi-\sigma^*$ electronic transition in free iodine, is hypsochromically shifted due to its complexation with the donor. 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

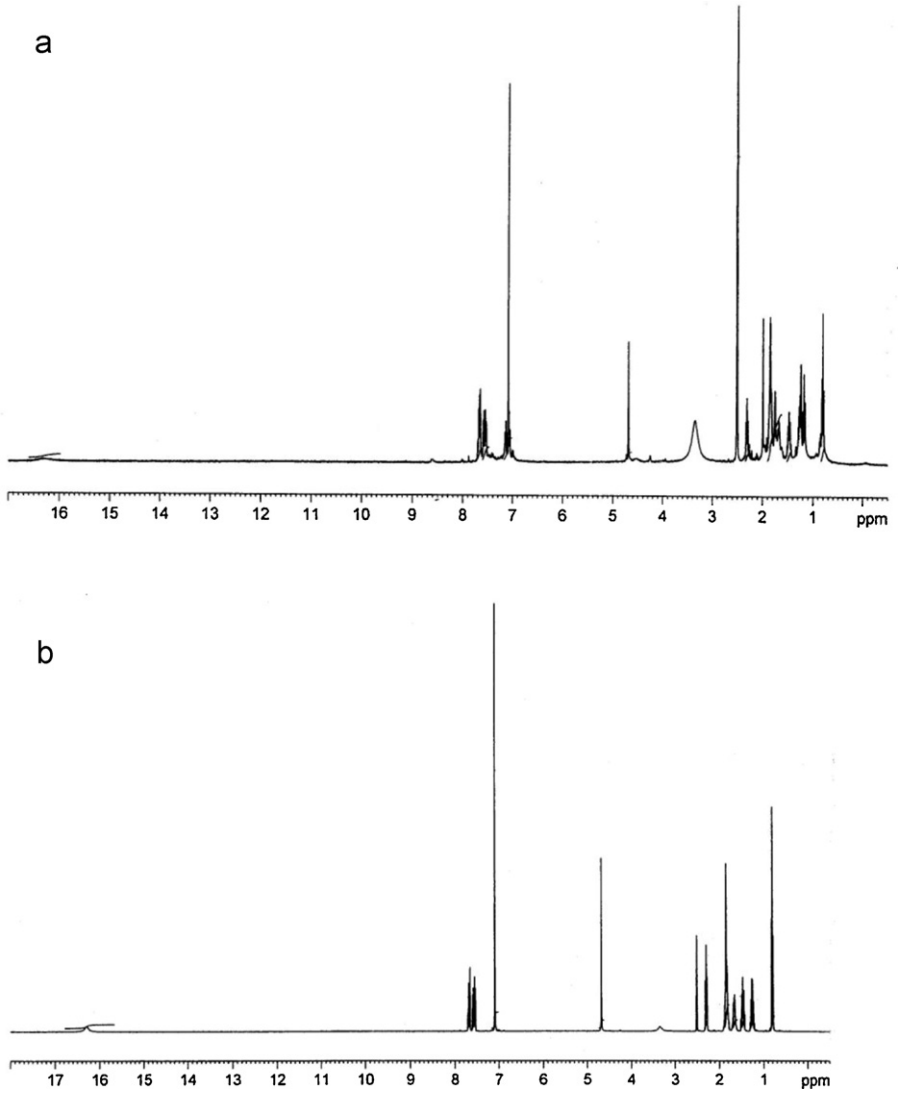


Fig. 1. ^{1}H NMR spectrum of (a) IRB–DDQ complex and (b) pure IRB.

to consider that 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 triiodide ion in solution. Parallel observations were made by several investigators in the study of molecular complexes of iodine with 2-aminopyrimidine [14], antipyrine [35], 4-amino-2,6-dimethylpyrimidine, 4-amino-5chloro-2,6-dimethylpyrimidine [36], etc. Such an observed variation in the electronic spectrum of the mixture indicated the interaction between the donor and the acceptor. The intensity of the band at 482 nm decreased while the intensity of the characteristic I_3^- ion band (360 nm) increased with elapse of time. 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 482 nm, as it reached a constant value quickly in majority of the solvents employed. A clear isosbestic point was observed at 442 nm (Fig. 3).

The observed time dependent electronic spectra of the system under investigation is due to a transformation of the initially formed outer 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 [14,25,35].

$$\text{Drug} + I_2 \leftrightharpoons \text{Drug}-I_2(\text{outercomplex}) \quad \text{Fast} \tag{1}$$

$$\text{Drug}-I_2 \leftrightharpoons [\text{Drug}-I]^+I^-(\text{innercomplex}) \quad \text{Slow} \tag{2}$$

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

The formation of triiodide ion (I_3^-) was confirmed by laser Raman spectrum of the complex. Raman spectroscopy can give valuable information on the nature and structural features of polyiodide anions. A representative laser Raman spectrum is given in Fig. 4. The results provided in Table 1 showed that the peaks at 143, 113, and 76 cm^{-1} corresponds to ν_{as}(I–I), ν_s(I–I), and $\delta(I_3^-)$, respectively and these peaks are due to the presence of I_3^- ion in irbesartan–iodine complex [16]. In the linear and symmetric I_3^- species the Raman active symmetric stretch (ν_s) occurs

Table 1
Raman bands observed for the irbesartan–iodine complex.

Compound	Assignments			References
	ν_{as}(I–I)	ν_s(I–I)	$\delta(I_3^-)$	
Povidone	147	104	86	[16]
Polyiodides	130–155	100–120	75	[37]
TACTD	147	108	85	[38]
DBTODAOD	147	108	–	[39]
Atenolol	153	102	85	[40]
Irbesartan	143	113	76	Present work

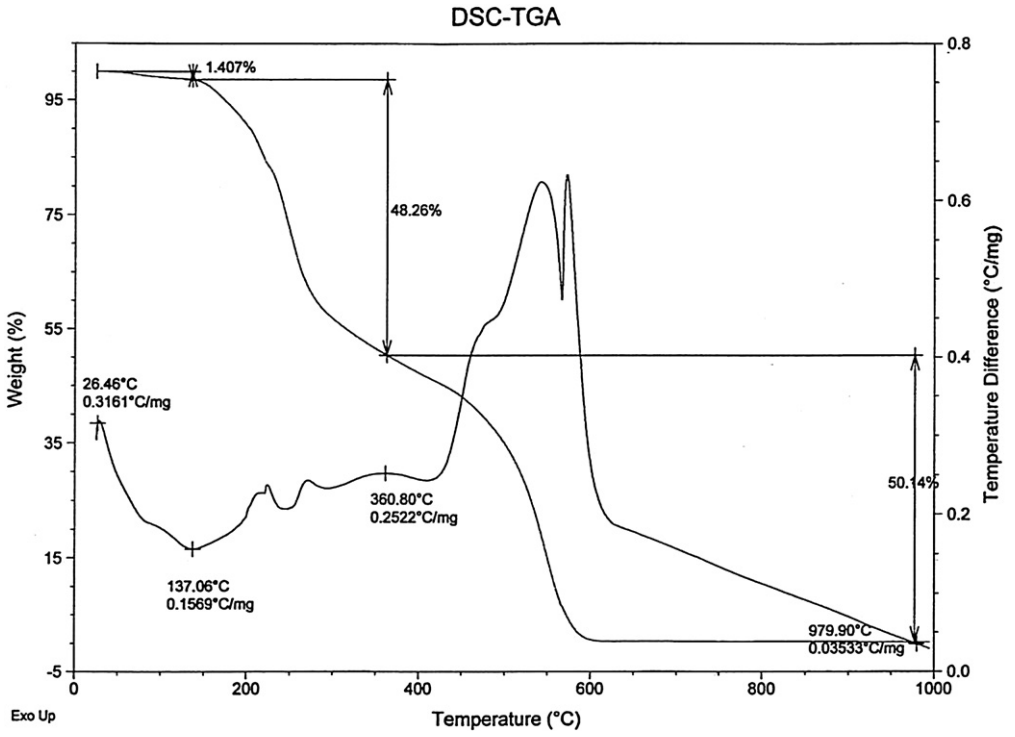


Fig. 2. DSC–TGA curve of the IRB–I_2 complex.

in the region of 100–120 cm^{-1}, while the antisymmetric stretch (ν_{as}) in 130–155 cm^{-1} range. The bending (δ) deformation become Raman active, for asymmetric I_3^- ion, in the region of near 80 cm^{-1} [26,29,37,38]. The observed Raman spectrum, in the present case, confirmed the formation of asymmetric triiodide ion as shown in the scheme given above.

The pseudo-first-order rate constants, k_1, were evaluated by employing the increase in absorbance of 360 nm band at different temperatures and solvents. The pseudo-first-order rate constants as a function of [D] and [A] are given in Table 2. The pseudo-first order rate constants for the formation of the product were independent of initial concentrations of iodine indicating first order dependence in [I_2]. The k_1 values increased with an increase in [D] and a plot of log k versus log [D] is linear (r 0.99) with a slope of unity indicating unit order dependence in [D]. This was further supported by the constancy of second order rate constants, k_2.

The rate constants as a function of temperature and solvent along with thermodynamic parameters for the IRB–I_2 reaction are collected in Table 3. The k_1 values increased with an increase in the relative permittivity of the medium. It is evident from the plot of log k_1 versus ε_r (supplemental information Fig. 2S) that, particularly in the case of IRB–I_2 system, there is deviation from

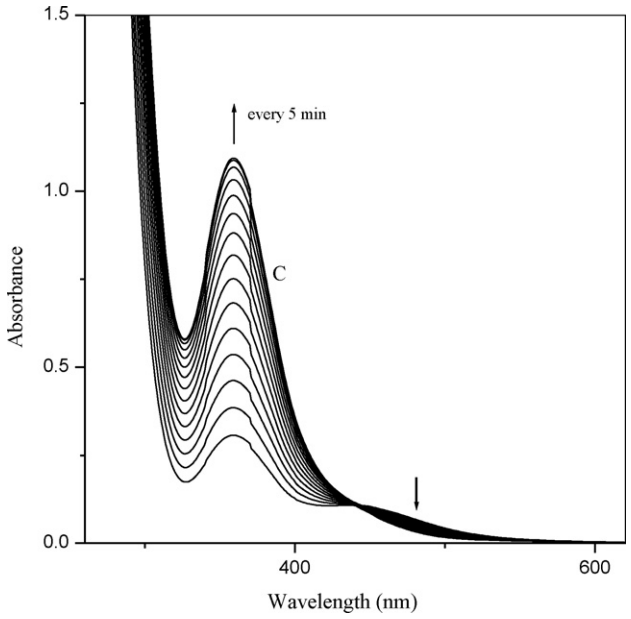


Fig. 3. Absorption spectra of Irbesartan with Iodine in *tert*-butyl alcohol at 298 K.

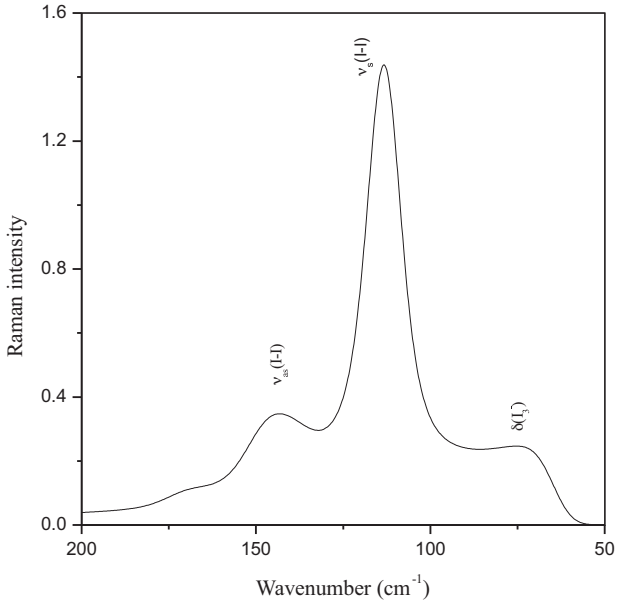


Fig. 4. Raman spectrum of the IRB–I_2 complex.

Table 2
Effect of concentration of donor and acceptor on the rate of the interaction at 298 K.

10^{-3} [D] (M)	10^{-5} [A] (M)	$10^4 k_1$ (s^{-1})	k_2 (s^{-1} mol^{-1} dm^3)
IRB–I_2 (in *tert*-butyl alcohol at 360 nm)			
0.50	1.25	10.6	2.1
0.75	1.25	16.1	2.1
1.00	1.25	21.2	2.1
1.25	1.25	26.5	2.2
1.25	1.00	28.3	
1.25	0.75	28.5	
1.25	0.50	29.0	
IRB–DDQ (in *tert*-butyl alcohol at 351 nm)			
1.00	1.25	1.2	0.1
1.50	1.25	1.8	0.1
2.00	1.25	2.3	0.1
2.50	1.25	2.9	0.1
2.50	1.00	2.6	
2.50	0.75	2.6	
2.50	0.50	2.6	

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. Thus, the only satisfactory correlation (r 0.933) in all likelihood may be as a result of specific solute–solvent–solvent interactions. This solvent dependence of k_1 values suggested that there might be a formation of a more polar transition state. Such a transition state is well supported by the large negative entropies of activation. Further, 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. There exists a linear correlation (supplemental information Fig. 3S, r 0.960) 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 3 indicated that a solvent change from chloroform to *tert*-butyl alcohol caused ~10-fold rate acceleration for the reaction which corresponds to a decrease in $\Delta G^{\#}$ of 5 kJ mol^{-1}.

3.4. Interaction of irbesartan with DDQ

The electronic absorption spectra of DDQ in the presence of a large excess of the donor, i.e. [D]/[A] > 100 was obtained as a function of time in different solvents. The electronic absorption spectra of the mixture of *tert*-butyl alcohol solutions of IRB and DDQ showed a new band at 578 nm, which is presumably be due to EDA complex between the donor and the acceptor (Fig. 5). The observed gradual decrease in the intensity of the band at 578 nm could be due to the consumption of the EDA complex, while the continuous increase of the 351 nm band with elapse of time is indicative of the formation of an ion-pair [39]. 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 [15]. A clear isosbestic point at 538 nm was also observed.

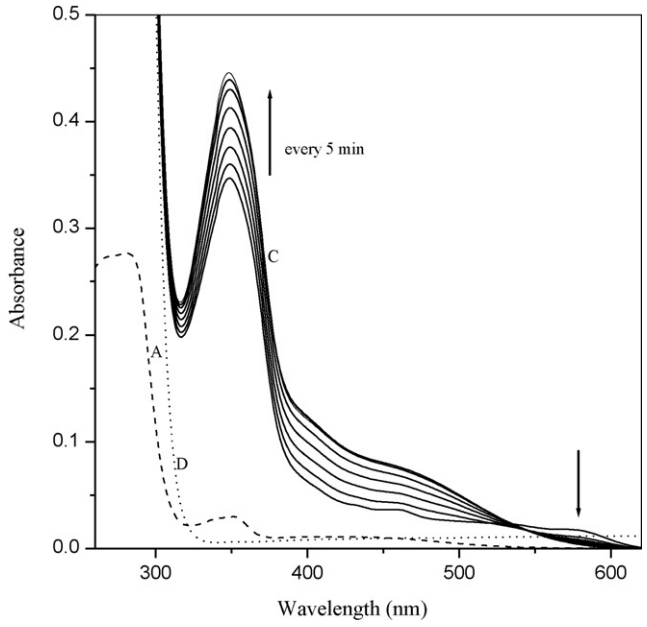


Fig. 5. Absorbance spectra for the Irbesartan with DDQ system in *tert*-butylalcohol at 298 K.

In order to obtain further information about the kinetics and mechanism of the interaction of DDQ with irbesartan, the increase in absorbance at 351 nm 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 CT complex as a function of [D] and [A] are also collected in Table 3. It is evident from the results that the rate is independent of initial concentration of DDQ indicating first order dependence on [A]. The plot of log k_1 versus log [D] is linear with a slope of unity (r 0.99; slope 0.99) indicating unit order dependence in [D]. This was further supported by the constancy in k_2 values [29].

As discussed earlier in the IRB–I_2 system, the effect of solvent on the reaction between the drug and DDQ was also investigated. Hereto, increase in polarity of the solvent could enhance the contribution of dative state and hence lead to a stronger charge transfer [40]. The results of effect of solvent (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. Involvement of such a polar transition state is well supported by the large negative entropies of activation. Also the 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. The correlation between $\Delta H^{\#}$ and $\Delta S^{\#}$ values was found to be linear (supplemental information Fig. 3S, r 0.999) indicating the operation of a common mechanism in the solvents investigated.

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

Solvent	ε_r[a]	λ (nm)	$10^4 k_1$ (s^{-1})			(H#	-(S#	(G#
			298 K	305 K	313 K			
Chloroform	4.90	360	2.4	2.9	3.3	14	268	93
1,2-Dichloroethane	10.36	364	5.6	5.9	6.4	5	290	91
tert-Butyl alcohol	12.47	361	20	26	29	17	240	88

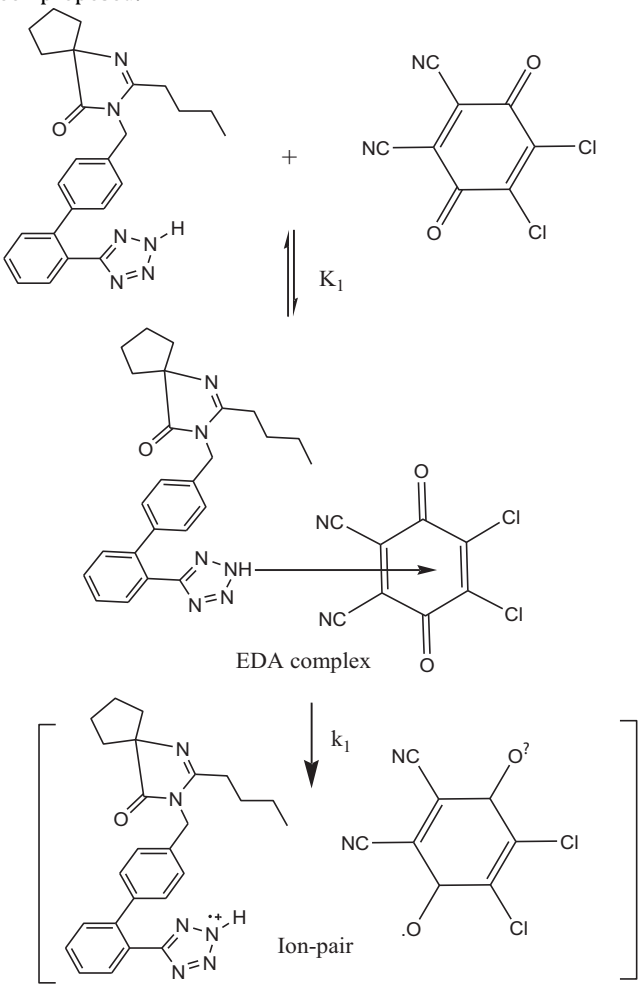
$\Delta H^{\#}$, kJ mol^{-1}; $\Delta S^{\#}$, J K^{-1} mol^{-1}; and $\Delta G^{\#}$, kJ mol^{-1}.
[a] ε_r, relative permittivity of the medium.

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

Solvent	ε_r[a]	λ (nm)	$10^4 k_1$ (s^{-1})			$\Delta H^{\#}$	$-\Delta S^{\#}$	$\Delta G^{\#}$
			298 K	305 K	313 K			
Chloroform	4.90	350	2.0	2.2	3.5	27	226	94
1,2-Dichloroethane	10.36	382	2.7	3.2	5.6	36	195	94
tert-Butyl alcohol	12.47	348	2.8	3.2	3.6	9	282	93

$\Delta H^{\#}$, kJ mol^{-1}; $\Delta S^{\#}$, J K^{-1} mol^{-1}; and $\Delta G^{\#}$, kJ mol^{-1}.
[a] ε_r, relative permittivity of the medium.

Based on the foregoing results and discussions the following plausible mechanism for the interaction DDQ with irbesartan has been proposed.



The above mechanism leads to the following rate law.

$$\frac{d[\text{ion-pair}]}{dt} = k_1\,[\text{EDA complex}]$$

or

$$\frac{d[\text{ion}-\text{pair}]}{dt} = k\,[\text{DDQ}]\,[\text{Drug}]$$

where $k = k_1K_1$

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

3.5. Characteristics of the CT complexes

In both IRB–I_2 and IRB–DDQ systems, an attempt was made to characterize the CT complexes formed in these reactions. For that the absorbance of the new bands 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 using the Scott equation [41]. A representative Scott plot is shown in supplemental information Fig. 4S and the values of K and ε determined are given in Table 5. The observed high values of K suggested that the formed CT complexes are of a strong type [13] and the linearity of the Scott plots further supports this result. The electronic spectra of drug/acceptor systems were recorded with varying [D] and constant [A]. Representative spectra are shown in Figs. 6 and 7 for drug/iodine and drug/DDQ systems, respectively. The nature of the spectra indicated that the interactions between the donor and the acceptor are of CT type.

Table 5
Spectral properties of the CT complexes formed between the irbesartan with DDQ and iodine in *tert*-butyl alcohol solvent at 298 K.

Property	DDQ	Iodine
λ_{max} (nm)	574	361
$h\nu_{CT}$ (eV)	2.16	3.43
$10^{14}\ \nu_{max}$ (s^{-1})	5.22	8.31
Formation constant, K ($dm^3\ mol^{-1}$)	4244	1210
Extinction coefficient, log ε ($dm^3\ mol^{-1}\ cm^{-1}$)	3.42	3.88
Oscillator strength, f	0.014	0.163
Dipole moment, μ	1.28	3.46
Ionization potential (eV)	8.40	8.13
Dissociation energy (eV)	4.30	1.62

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 [42] 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 [42–44]. Out of the many applications of CT complexes, one important application is to calculate the ionization potential of the donor. The ionization potential (I_p) 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 Pignataro [31,42].

$$I_p(\text{eV}) = 5.76 + 1.52 \times 10^{-4}\bar{\nu}_{\text{DDQ}}\,(\text{cm}^{-1}) \quad (9)$$

$$I_p(\text{eV}) = 2.90 + 1.89 \times 10^{-4}\bar{\nu}_{\text{Iodine}}\,(\text{cm}^{-1}) \quad (10)$$

The calculated I_p value for molecular orbital participating in CT interaction of the drug is listed in Table 5. 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. The dissociation energies of the complex were

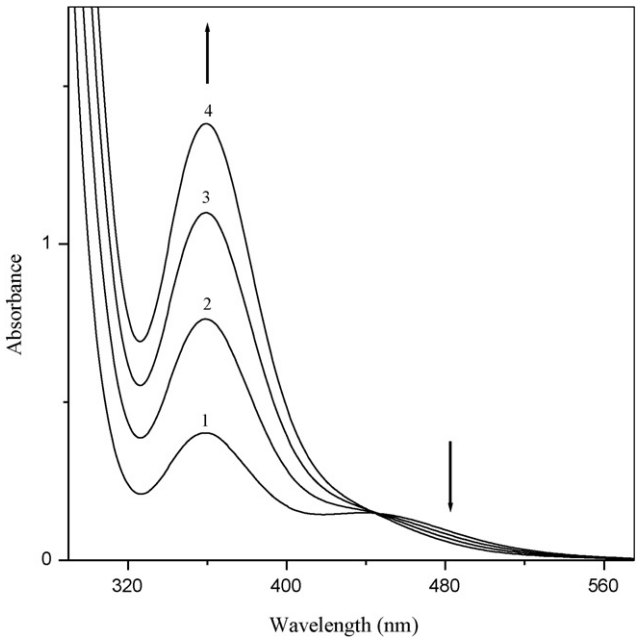


Fig. 6. Concentration variation spectra for the irbesartan – iodine system in *tert*-butyl alcohol at 298 K [A] = 1.25×10^{-4} M; [D]: (1) 0.50, (2) 0.75, (3) 1.00 and (4) 1.25×10^{-3} M.

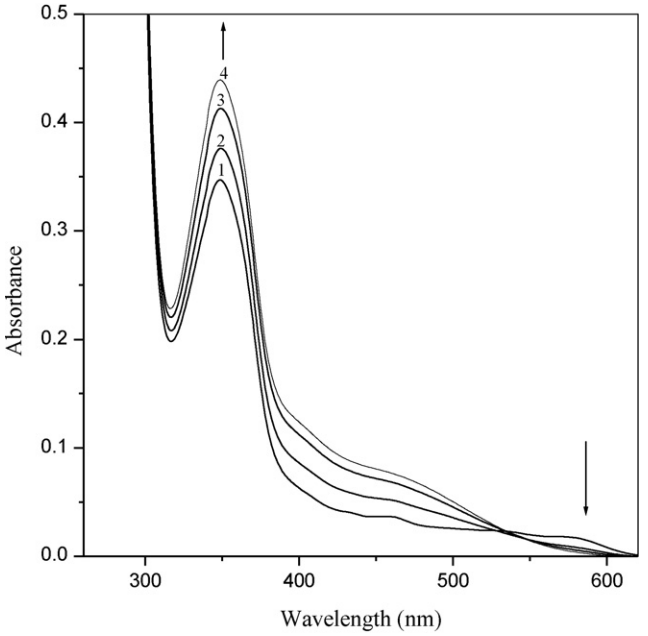


Fig. 7. Concentration variation spectra for the irbesartan - DDQ system in *tert*-butyl alcohol at 298 K [A] = 1.25×10^{-4} M; [D]: (1) 1.00, (2) 1.50 (3) 2.00 and (4) 2.50×10^{-3} M.

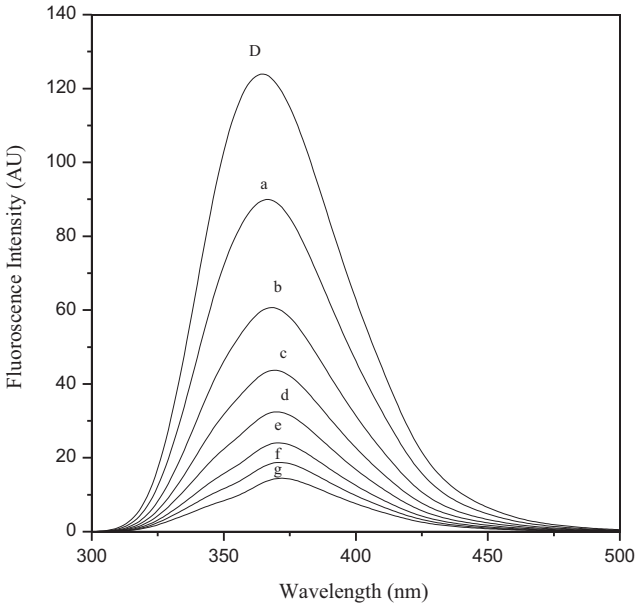


Fig. 8. Fluroscence spectra for IRB–DDQ system in dichloroethane at fixed concentration of [D] = {6.25×10^{-4} (curve D)} and variable concentration of [A] $\times 10^{-6}$ = {3.125 (curve a), 6.25 (curve b), 9.375 (curve c), 12.5 (curve d), 15.625 (curve e), 18.75(curve f), 21.875 (curve g)} mol L^{-1} at 298 K.

calculated as described earlier [43] and the calculated values of W (Table 6) suggested that the investigated complex is reasonably strong and stable under the studied conditions with higher resonance stabilization energy [13].

3.6. Fluorescence quenching studies

The nature and magnitude of the interaction of drugs with receptors play an important role in the pharmacokinetics of the drugs. CT interaction is one of the non covalent binding forces in the drug–receptor mechanism. In the present study, an attempt was made to study the CT interaction of IRB with DDQ and iodine by means of fluorescence study. Fluorescence spectra were recorded at room temperature in different solvents in the range of 300–700 nm using an excitation at 280 nm. It was observed the fluorescence of IRB was quenched by both DDQ and iodine as a result of formation of CT complex. The experimental results indicated that the quenching efficiency increased with increasing concentration of the electron acceptors (Figs. 8 and 9), increasing time (Figs. 10 and 11) and also with an increase in the relative permittivity of the medium. The fraction of acceptors bound to IRB (θ) was determined by using the following equation.

$$\theta = \frac{F_0 - F}{F_0} \tag{11}$$

where F and F_0 denote the fluorescence intensities of IRB in the presence of acceptor and in the absence of acceptor, respectively. From the resulting values of θ, the association constant K_f for IRB–DDQ and IRB–iodine systems was computed using the method described by Ward [45]. It has been shown that for equivalent and independent binding sites:

$$\frac{1}{(1-\theta)K_f} = \frac{[A_T]}{\theta - n\,[D_T]} \tag{12}$$

where n is the number of binding sites, $[A_T]$ is the total acceptor concentration and $[D_T]$ is the total donor concentration. The plot $1/(1-\theta)$ versus $[A_T]/\theta$ is linear (r 0.992 for IRB–DDQ system and r 0.994 for IRB–iodine system) indicating that under the experimental conditions all the binding sites are equivalent and independent. The value of K_f obtained, from the plots, for

Table 6
Binding constants (K_A) and number of binding sites (n) for IRB–DDQ and IRB–iodine systems in different solvents.

Solvent	IRB–DDQ system		IRB–iodine system	
	K_A (mol^{-1} L)	n	K_A (mol^{-1} L)	n
Chloroform	9×10^5	1.4	0.1×10^3	0.7
Dichloroethane	45×10^5	1.5	5×10^3	1.0
tert-Butyl alcohol	55×10^5	1.6	115×10^3	1.2

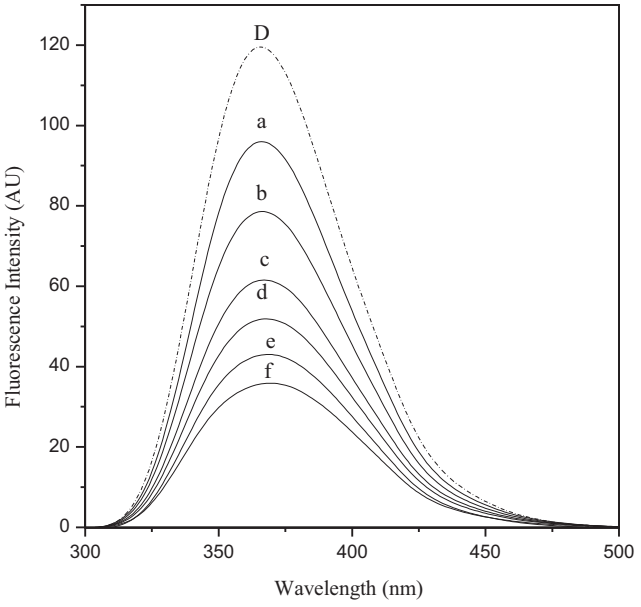


Fig. 9. Variation of fluorescence spectra of IRB–iodine system in *tert*-butyl alcohol at fixed concentration [D] = {3.125×10^{-4} (curve D)} and variable concentration of [A] $\times 10^{-6}$ = {3.125 (curve a), 6.25 (curve b), 9.375 (curve c), 12.5 (curve d), 15.625 (curve e), 18.75(curve f)} mol L^{-1} at 298 K.

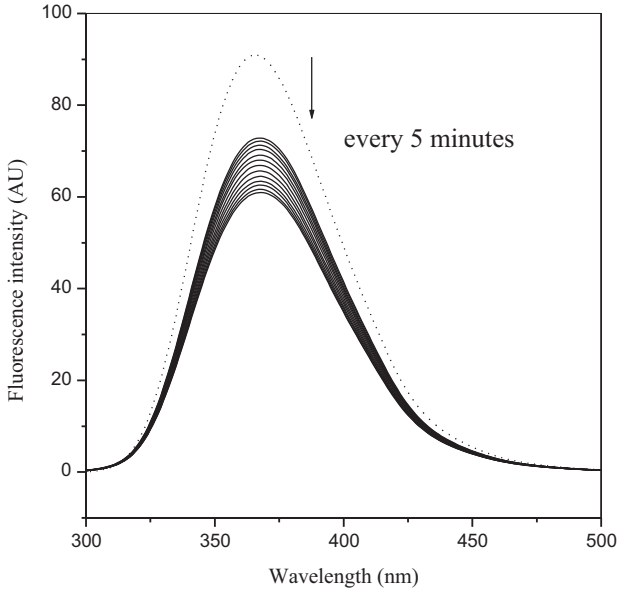


Fig. 10. Variation of fluorescence spectra of IRB–DDQ system in *tert*-butyl alcohol at 298 K.

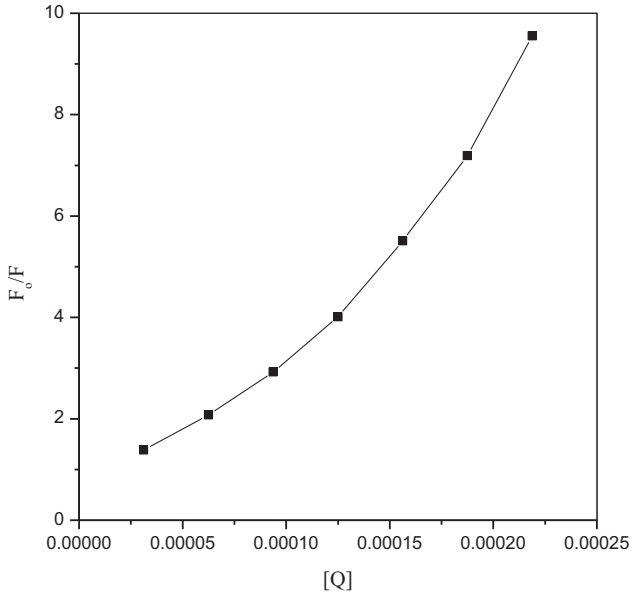


Fig. 12. Stern–Volmer plot for the fluorescence quenching of IRB with DDQ in dichloroethane at 298 K.

IRB–DDQ and IRB–iodine systems are found to be 5.9×10^4 and 1.9×10^4 mol L^{-1}, respectively. The standard Gibbs energy change ΔG° was calculated from K_f using the relation $\Delta G^\circ = -2.303$ RT $\log_{10} K_f$. The ΔG° values for IRB–DDQ and IRB–iodine systems were found to be -27 and -25 kJ mol^{-1}, respectively, indicating spontaneous interaction between the drug and the acceptors.

Fluorescence quenching can occur by different mechanisms viz. static or dynamic or both. Stern–Volmer equation (Eq. (13)) is useful in understanding the mechanism of fluorescence quenching.

$$\frac{F_0}{F} = 1 + K_{SV}[Q] \tag{13}$$

where F_0 is the initial fluorescence intensity measured in the absence of quencher and F is the fluorescence intensity in the presence of quencher concentration [Q]. The Stern–Volmer constant K_{SV} is obtained by plotting F_0/F against [Q]. The Stern–Volmer plot showed positive deviation for IRB–DDQ system (Fig. 12) while linear in the case of IRB–iodine system (Fig. 13). In the case of IRB–DDQ system, the positive deviation observed, at higher concentrations of the quencher, may be due to the simultaneous presence of dynamic and static quenching mechanisms. In the case of IRB–iodine system, the linear Stern–Volmer relationship observed indicated that either static or dynamic quenching is dominant [46,47]. The red shift (365–371 nm) observed in the IRB–DDQ system, during the quenching process, may be due to the decrease in hydrophobicity of the microenvironment of the binding region [48].

The relationship between the fluorescence quenching intensity and the concentration of quenchers can be described by the following equation.

$$\log_{10}\frac{F_0 - F}{F} = \log K_A + n \log_{10}[Q] \tag{14}$$

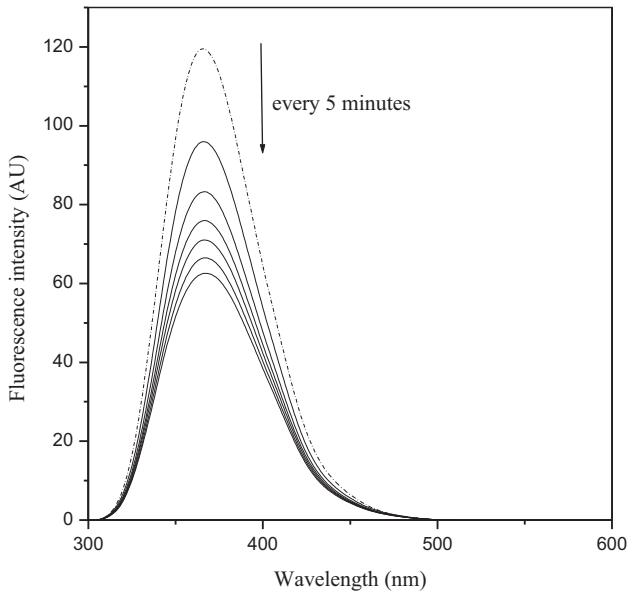


Fig. 11. Variation of fluorescence spectra of IRB–iodine system in *tert*-butyl alcohol at 298 K.

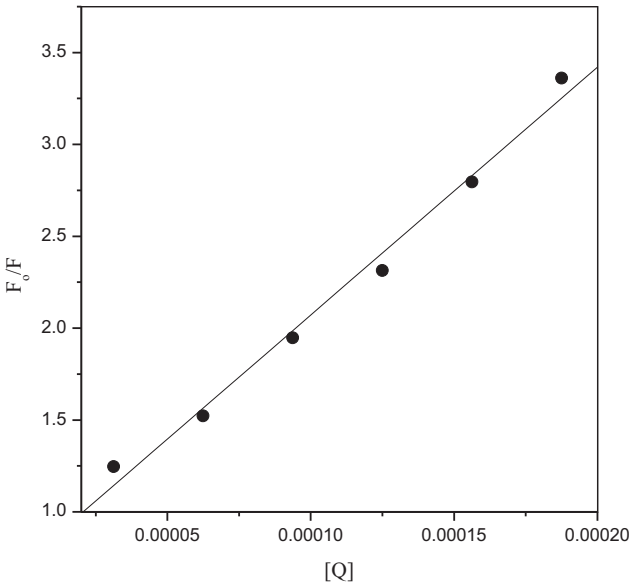


Fig. 13. Stern–Volmer plot for the fluorescence quenching of IRB with iodine in *tert*-butyl alcohol at 298 K.

where K_A is the binding constant and n is the number of binding sites per IRB [49]. In the present study, in both the case, a plot of $\log_{10}(F_0-F)/F$ versus $\log_{10}$ [Q] is linear (supplemental information Figs. 5S and 6S) and the binding constant values computed are collected in Table 6. The results indicated that, in both the systems, the binding constant value increased with an increase in polarity of the medium. This is due to the fact that increase in polarity of the medium would stabilize the charge separation relatively better leading to stronger binding between the reactants. Also, the magnitude of binding constant in IRB–DDQ system is higher than that in IRB–iodine system. These observations are in corroboration with the results of absorption spectral studies as enumerated earlier in this paper. That is the formation constant (Table 5) and dissociation energy of IRB–DDQ system is higher than that for the other system. Also, the rate constant for the interaction, in both the cases, increased with an increase in polarity of the medium (Tables 3 and 4). The value of *n*, for a given system, is nearly constant in different solvents indicating the presence of equivalent binding sites.

4. Conclusions

Spectroscopic and spectrofluorimetric studies on the interaction of iodine and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone with irbesartan revealed that the interaction was found to proceed through the formation of an outer complex and its conversion to CT complex. 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 irbesartan–I_2 system was characterized by the formation of triiodide ion, which was confirmed by Raman spectrum. The rate of the reaction computed through absorption spectroscopic technique and the binding constant calculated using spectrofluorimetric studies were observed to increase with an increase in the relative permittivity of the medium. The mechanisms of the interaction of the drug studied may be useful in understanding the binding of the drug molecule in real pharmacokinetic study.

Acknowledgement

The authors thank the Council of Scientific and Industrial Research (CSIR), New Delhi for its financial assistance (01/2221/08) to carry out this research work.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.saa.2011.05.022.

References

[1] R.S. Mulliken, W.B. Person, Molecular Complexes – A Lecturer and Reprint Volume, Wiley & Sons, New York, 1969.
[2] R.S. Mulliken, J. Am. Chem. Soc. 74 (1952) 811–824.
[3] R. Foster, Charge Transfer Complex, Academic Press, London, 1969.
[4] A.M. Slifkin, Charge Transfer Interactions of Biomolecules, Academic Press, New York, 1971.
[5] M. Krishnamurthy, K.S. Babu, U. Muralikrishna, Indian J. Chem. 27A (1988) 669–672.
[6] M. Hasani, M. Shamsipur, J. Chem. Soc. Perkin Trans. 2 (1998) 1277–1282.
[7] M.E.M. Nour, Spectrochim. Acta A 56 (2000) 167–170.
[8] A.H. Al-Taiar, M.A. Al-Emabe, F.A. Al-Mashadane, M. Hadjel, J. Coord. Chem. 55 (2002) 1143–1146.
[9] M.S. Liao, Y. Lu, V.D. Parker, S. Scheiner, J. Phys. Chem. A 107 (2003) 8939–8948.
[10] M.M.A. Hamed, E.M. Abdalla, Sh.M. Bayoumi, Spect. Lett. 36 (2003) 357–373.
[11] G.M. Neelgund, A.S. Kulkarni, M.L. Budni, Monatshefte Chemie 135 (2004) 343–355.
[12] N.A. Al-Hashimi, K.A. Hassan, El-Metwally Nour, Spectrochim. Acta A 62 (2005) 317–321.
[13] M. Pandeeswaran, K.P. Elango, Spectrochim. Acta 65A (2006) 1148–1153.
[14] U.M. Rabie, M.H. Ab-El-wafa, R.A. Mohamed, J. Mol. Struct. 871 (2007) 6–13.
[15] M. Pandeeswaran, K.P. Elango, Spectrochim. Acta 69A (2008) 1082–1088.
[16] M. Pandeeswaran, K.P. Elango, Spectrochim. Acta A 72 (2009) 789–795.
[17] R.A. Marcus, Rev. Mod. Phys. 65 (1993) 599–610.
[18] I.M. Khan, A. Ahmad, Spectrochim. Acta A 73 (2009) 966–971.
[19] N. Martin, J.L. Segura, C. Seoane, J. Mater. Chem. 9 (1997) 1661–1676.
[20] M. Lizuka, Y. Shiratori, S. Kuniyoshi, K. Kudo, K. Tanaka, 130–132, Appl. Surf. Sci. (1998) 914–918.
[21] M. Goes, J.W. Verhoeven, H. Hofstraat, K. Brunner, Chem. Phys. Chem. 4 (2003) 349–358.
[22] R. Dabestani, K.J. Reszka, M.E. Sigman, J. Photochem. Photobiol. A 117 (1988) 223–233.
[23] R. Jakbiak, Z. Bao, L. Rathberg, Synth. Met. 114 (2000) 61–64.
[24] P. Pal, S. Bhattacharya, A.K. Mukherjee, D.C. Mukherjee, Spectrochim. Acta A 61 (2005) 879–885.
[25] E.M. Nour, L.A. Shahada, S.A. Sadeek, S.M. Teleb, Spectrochim. Acta A 51 (1995) 471–474.
[26] E.M. Nour, L.H. Chen, J. Lanne, J. Phys. Chem. 90 (1986) 2841–2846.
[27] R.P. Simondsen, G. Tollin, Mol. Cell. Biochem. 33 (1980) 13–24.
[28] K.F. Croom, M.P. Curran, K.L. Goa, C.M. Perry, Drugs 64 (2004) 999–1028.
[29] M. Pandeeswaran, K.P. Elango. J. Sol. Chem. doi:10.1007/s10953-009-9467-3.
[30] P. Job, Ann. Chim. Phys. 9 (1928) 113–203.
[31] M. Gaber, S.S. Al-Shihry, Spectrochim. Acta A 62 (2005) 526–531.
[32] M.S. Refat, A.M. El-Didamony, Spectrochim. Acta A 65 (2006) 1148–1153.
[33] D.K. Sau, R.J. Butcher, S. Chaudhuri, N. Saha, Polyhedron 23 (2004) 5–14.
[34] M. Ayad, S. Belal, A.A.Et. Kheir, S.Et. Adl, Talanta 34 (1987) 793–797.
[35] M. Hasani, A. Rezaei, Spectrochim. Acta A 65 (2006) 1093–1097.
[36] U.M. Rabie, R.A. Mohamed, M.H. Ab-El-wafa, Spectrochim. Acta A 68 (2007) 605–611.
[37] E.M. Nour, L.A. Shahada, Spectrochim. Acta A 45 (1989) 1033–1035.
[38] E.M. El-Neema, Spectrochim. Acta A 60 (2004) 3181–3185.
[39] M. Hasani, S. Akbari, Spectrochim. Acta A 68 (2007) 409–413.
[40] Z. Rappoport, J. Chem. Soc. (1963) 4498–4512.
[41] R.L. Scott, Recl. Trav. Chim. Pays-Bas Belg. 75 (1956) 787–789.
[42] G.G. Aloisi, S. Pignataro, J. Chem. Soc. Faraday Trans. 69 (1973) 534–539.
[43] M. Pandeeswaran, K.P. Elango, Spectrochim. Acta A 65 (2006) 1148–1153.
[44] H.M. McConnel, J.J. Ham, J.R. Platt, J. Am. Chem. Soc. 21 (1953) 66–71.
[45] L.D. Ward, Method. Enzymol. 17 (1985) 400–415.
[46] J.S. Park, J.N. Wilson, K.I. Hardcastle, U.H.F. Burnz, M. Srinivasarao, J. Am. Chem. Soc. 128 (2006) 7714–7715.
[47] Q. Zhou, T.M. Swager, J. Am. Chem. Soc. 117 (1995) 12593–12602.
[48] N. Seedher, P. Agarwal, J. Lumin. 130 (2010) 1841–1848.
[49] H. Xu, Q. Liu, Y. Zuo, Y. Bi, S. Gao, J. Sol. Chem. 38 (2009) 15–25.