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ORIGINAL PAPER

On the Photophysicochemical Properties of Selected Fluoroquinolones: Solvatochromic and Fluorescence Spectroscopy Study

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Abstract The photophysicochemical properties of selected fluoroquinolones in different solvents of various physical properties, including polarity and hydrogen bonding ability, were investigated using steady state fluorescence spectroscopy. The solvent-dependant fluorescence emission spectra of selected fluoroquinolones, namely ciprofloxacin (CIPR) and enrofloxacin (ENRO), were employed to gain insights concerning its photophysicochemical properties of interests. Interestingly, fluorescence spectra of the selected drugs exhibited structured emission spectra in nonpolar solvents such as hexane, whereas unstructured spectra were observed in more polar solvents such as alcohols and water. Also, a notable bathochromic shift in $\lambda_{\max}^{em}$ was observed in fluorescence spectra of both drugs with increasing solvent polarity that resulted in biphasic behavior upon applying the Lippert-Mataga correlation that correspond to general and specific solvent effects. Applying the Lippert-Mataga correlation to the fluorescence spectra of CIPR and ENRO in various solvents was employed to estimate the dipole moment difference between the ground and excited states of them, $\Delta\mu\ (\mu_e - \mu_g)$, where obtained results revealed the values of 9.4 and 16.2 Debye for the LE and ICT states of ENRO, respectively, and 8.0 and 16.2 Debye for the LE and ICT states of CIPR, respectively. Multiple linear regression analysis (MLRA) based on Kamlet-Taft equating was applied against absorption frequency (ν_{abs}), emission frequency (ν_{em}), Stokes shift ($\Delta\nu$), and fluorescence quantum yield (Φ_f), where obtained results revealed excellent correlation (R: 0.916–0.966) that are consistent with other results considering the effect of solvent polarizability, hydrogen bonding ability, and viscosity on the photophysicochemical properties of the studied fluoroquinolones.

Keywords Fluoroquinolones · Fluorescence · Solvatochromism · Lippert-Mataga correlation · Kamlet-Taft equation · Multiple linear regression analysis

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Introduction

Global warming has triggered tremendous amount of efforts toward minimizing its effects and anticipating its consequences on various aspects of our lives including health related dilemma [1–4]. Hence, the high level of radiation that is currently reaching the earth plays a notable role in such observed consequences of global warming [1–4], which in turn affects the physicochemical behavior of wide range of chemicals and materials that are widely used in various applications; this includes pharmaceutical materials, such as drugs. It is well known that molecules behave differently when they exist in their excited state in comparison to their behavior in the ground state, where these excited states result from absorption of different kinds of radiation including sunlight [5–7]. One of the main issues related to this behavior is the unexpected chemical reactivity of these excited chemical species, where such matter is of particular importance in pharmaceutical therapy in case of administrating photosensitive drugs [7–10]. On the other hand, it is noteworthy mentioning that there is currently a wide range of pharmaceutical formulations that are considered as photosensitive materials, where investigating their photo-physicochemical behavior is still needed.

In general, the physicochemical behavior of photosensitive chemical specie is linked with the dipole moment that

the chemical specie possesses in its excited state (μ_{ex}), and hence concluding the μ_{ex} can be utilized for exploring the physicochemical behavior of photosensitive materials, including pharmaceutical materials. Importantly, photosensitive pharmaceutical formulations are predictably subjected to be metabolized through unexpected pharmacokinetics pathway upon being exposed to various kinds of radiation. Therefore, there is a necessity for exploring the photophysicochemical behavior of wide spectrum of pharmaceutical materials that are currently available in the market and widely prescribed; among these pharmaceutical materials are fluoroquinolone-based antibiotics [11, 12]. Fluoroquinolones (FQs) are a class of synthetic antibacterial agents that possess a wide spectrum of activity against gram-negative and gram-positive bacteria and frequently used for veterinary and human medication. However, one of the main concerns associated with this class of antibiotics is their phototoxicity, which in turn is attributed to their photophysiochemical properties [12–14]. Structurally they have in common a quinolone moiety with fluorine atom as a substituent at position C-6, where the quinolone moiety is responsible for most of the absorption and emission spectral properties of FQs.

Recently, several reports have demonstrated that several members of FQs, such as oflofloxacin and ciprofloxacin [15–18], possess a phototoxicity that is mainly driven by their photophysicochemical activities. In parallel to phototoxicity studies, other reports can be located in the literature concerning the photophysical and photochemical properties of various members of FQs. However, there is still a need for widening the spectrum of those members of FQs, such as enrofloxacin (ENRO) and ciprofloxacin (CIPR). 3-D structure of ENRO is shown in Fig. 1. Both drugs are synthetic chemotherapeutic antibiotic that exhibits antibacterial activities against a broad spectrum of gram- positive and gram-negative bacteria, whose photophysicochemical properties need to be explored via using different approach or even to be studied in more details these important properties. On the other hand, it is noteworthy mentioning that solvatochromism is one of the most frequently utilized approaches that are frequently employed for exploring the photophysicochemical properties of photo sensitive materials, including pharmaceutical materials [19–25]. Principally, the electronic absorption or emission spectra of a substance of interest are generated in different media of different polarity and acidity, where the media-dependent spectral properties are employed for gaining insights concerning the photophysicochemical properties of this substance.

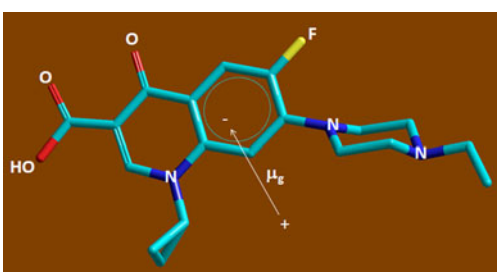

Fig. 1 Optimized 3-D geometry of ENRO; the arrow indicates the direction of dipole moment in the ground state (μ_g)

In the view of the growing interests directed toward the importance of phototoxicity of pharmaceutical materials, we investigate in this study the effect of solvent's polarity on the photophysicochemical properties of a selected Fluoroquinolones drug, namely ENRO and CIPR. Electronic absorption and emission spectra, fluorescence in particular, were collected in solvents of different polarities that exhibit various solvatochromic parameters, such as normalized polarity parameter ($E_T(30)$) dipolarity/polarizability (π^*), hydrogen-bond donor acidity (α), and hydrogen-bond acceptor basicity (β), where these spectra were interpreted in a fashion that can relieve insights concerning the photophysicochemical properties of both drugs .

Experimental

Apparatus

The electronic absorption and steady state fluorescence spectra were recorded on 100 Conc spectrophotometer (Cary) and RF-5301PC spectrofluorimeter (Shimadzu) equipped with a 150 W xenon lamp, respectively. All spectra were collected using 1.0 cm quartz cuvettes. Fluorescence spectra were generated with both excitation and emission bandwidths set on 5 nm and an excitation wavelength that corresponds to λ_{max} observed in the absorption spectrum of each solvent.

Materials and Procedure

ENRO, CIPR and quinine sulfate were obtained from Sigma-Aldrich, whereas all solvents were purchased from either Acros Organics or Sigma-Aldrich. All materials were used without further purification and aqueous solutions were prepared using Milli-Q ultrapure water (18 MΩ). Stock solution of each drug with concentration of 2×10^{-4} M was prepared in Methanol and kept at 278 K till needed. Solutions in different solvents were prepared by withdrawing an aliquot of the drug stock solution (in methanol), then evaporating the methanol followed by re-dissolving the solid residue with the solvent of interest. Solutions for quantum yield calculations were prepared with Absorbance at $\lambda_{ex}\leq0.05$. Fluorescence quantum yield (Φ_f) calculation was performed using quinine sulfate (in 0.1 N sulfuric acid) as a reference material ($\Phi_f=0.52$, $\lambda_{ex}=360$ nm) [5].

Table 1 Summary of Solvents' physical parameters and absorption and fluorescence spectra of ENRO and CIPR

Solvent	n	ε	Δf	$E_T(30)$	Viscosity	α	β	π*	λ_{max}(nm)		λ_{em}(nm)		Stokes Shif(Δv),cm^{-1}		ϕ_f	
				Kcal.mol-1	cp(mPa.s)				CIPR	ENRO	CIPR	ENRO	CIPR	ENRO	CIPR	ENRO
Polar protic																
Water	1.333	80.1	0.320	63.100	0.89	1.17	0.47	1.09	274	274	446	446	14,075	14,075	0.249	0.249
Isopropanol	1.378	20.2	0.276	48.400	2.04	0.76	0.84	0.48	282	280	434	435	12,420	13,039	0.013	0.116
Methanol	1.326	32.7	0.310	55.400	0.54	0.98	0.66	0.60	280	280	441	435	13,039	12,726	0.116	0.024
Ethanol	1.330	25.3	0.301	51.900	1.07	0.86	0.75	0.54	280	282	435	434	12,726	12,420	0.024	0.013
1-propanol	1.385	20.8	0.275	50.700	1.95	0.84	0.90	0.52	280	280	429	429	12,404	12,404	0.022	0.022
1-butanol	1.399	17.8	0.264	49.700	2.54	0.79	0.84	0.40	280	280	429	429	12,404	12,404	0.018	0.018
2-butanol	1.398	17.3	0.263	47.100	3.10	0.69	0.80	0.40	278	278	428	428	12,607	12,607	0.015	0.015
Ethylene Glycol	1.432	41.4	0.276	56.300	16.10	0.90	0.52	0.92	280	280	449	449	13,443	13,443	0.398	0.398
Polar aprotic																
Ethyl acetate	1.372	6.1	0.201	38.100	0.42	0.00	0.45	0.55	282	282	426	426	11,937	11,987	0.024	0.024
DMF	1.431	38.3	0.275	43.200	0.79	0.00	0.69	0.88	282	282	437	437	12,578	12,578	0.015	0.015
DMSO	1.479	47.2	0.263	44.800	1.99	0.00	0.76	1.00	281	281	446	446	13,166	13,166	0.008	0.008
Acetonitrile	1.344	36.6	0.305	45.500	0.37	0.19	0.40	0.75	282	282	436	436	12,499	12,499	0.044	0.044
Dichloromethane	1.424	8.9	0.217	40.700	0.41	0.13	0.10	0.82	283	283	427	427	11,916	11,916	0.024	0.024
Nonpolar																
Chloroform	1.446	4.8	0.148	39.100	0.54	0.20	0.10	0.52	280	280	416	416	11,647	11,647	0.160	0.160
1.4-Dioxane	1.422	2.2	0.020	36.000	1.18	0.00	0.37	0.55	281	281	416	416	11,520	11,520	0.085	0.085

n Refractive index, *ε* Permittivity (dielectric constant), Δf Orientation polarizability, $E_T(30)$ Normalized polarity parameter, π^* Dipolarity/polarizability, β Hydrogen-bond acceptor basicity, α Hydrogen-bond donor acidity, λ_{ex} Excitation wavelength, λ_{max} Absorption maximum, λem Fluorescence emission maximum, ν_{em} Emission frequency, $\Delta\nu$ Stokes shift, ϕ_f Fluorescence quantum yield

Geometry Optimization & Quantum Mechanics Calculation

3-D structure optimization of the studied drugs and quantum mechanics calculation were conducted based on combination of semiemperical and molecular mechanics (MM+) calculations employing HyperChem 8.0 software package (HyperCube Inc., Gainesville, FL, USA).

Results and Discussion

It is noteworthy mentioning that almost similar results were obtained for both drugs under investigations upon performing different experiments and testing. Hence, most of the results presented herein are those obtained for ENRO, whilst those results obtained for CIPR are summarized in Tables 1 and 2, where CIPR graphical results are not presented in most conditions where there was no significant difference amongst the tested drugs. The electronic absorption and steady state fluorescence spectra of the selected fluoroquinolones were obtained in solvents of different polarities and hydrogen bonding capabilities, where both drugs are soluble in all of tested solvents with a concentration in the μM range. Table 1 summarizes the corresponding data of all these spectra in addition to solvents' physical parameters, this includes various solvation parameters, such as normalized polarity parameter ($E_T(30)$), dipolarity/polarizability (π^*), hydrogen-bond donor acidity (α), and hydrogen-bond acceptor basicity (β). As it can be noticed from Table 1, identical results were obtained for both drugs with negligible differences.

Normalized fluorescence emission spectra of ENRO in selected solvents are shown in Fig. 2, where as can be noticed there is a notable bathochromic shift of approximately 45 nm occurs in the fluorescence emission spectrum upon increasing solvent polarity and hydrogen bonding ability. On the other hand, it is worth pointing out that no correction was applied to the fluorescence spectra against the inner filter effect, where a negligible effect was observed upon calculating the fluorescence quantum yield, whereas shift observed in spectra is independent of this effect. Interestingly, not only a bathochromic shift is observed with increasing polarity, but also a notable change in the spectrum shape can be observed. In particular, two bands can be observed within an emission spectrum of ENRO at λ≈410 and 390 nm in nonpolar solvent, such as chloroform and dioxane, where these two bands start to exhibit a bathochromic shift and loosing the shape, respectively, with increasing the polarity of the solvent. For further confirmation of the existence of these two bands, the effect of n-hexane on the emission spectra of ENRO was investigated. As illustrated in Fig. 3, the band that appears at λ≈380 exhibits a full shape with increasing hexane level in the solution. Hence, such fading in the structured emission with increasing solvent polarity implies the occurrence of both general and specific solvent effects. In addition, the spectral shift observed as solvent's polarity increases can be attributed to the occurrence of potential intramolecular charge transfer (ICT) that is increasingly stabilized with increasing solvent polarity. Thus, the occurrence of ICT generates a dipole moment in the excited state across the ENRO molecule that is more stabilized in polar solvents. The effect of solvent polarity in terms of permittivity (dielectric constant) on λ_{max}^{em} of ENRO is illustrated in Fig. 4, where as can be noticed a dramatic increase in can be observed upon increasing solvent permittivity.

However, it is noteworthy mentioning that implementing only the solvent permittivity as scale for solvent polarity is inconclusive in terms of identifying the interaction between the fluorophore and the solvents. Thus, traditionally the effect of solvent polarity on fluorescence emission spectra of a fluorophore is investigated based to changes observed in Stokes shift $\Delta\mu$ ($\nu_{ex} - \nu_{em}$) and Φ_f in various solvents of different polarity. The effect of solvent polarity on Stokes shift of a fluorophore is commonly presented according to the Lippert-Mataga relationship, where this equation correlates the energy difference between absorption and emission

Table 2 Estimated values for the solvent independent coefficients, standard deviation, and correlation coefficient (R) obtained from MLRA employing Kamlet-Taft equation

XYZ		XYZ_o	a	b	c	d	R
Δν	CIPR	9,921±318	929±172	868±242	2,502±339	—	0.941
	ENRO	9,151±295	995±174	1,664±298	2,490±309	—	0.966
ν_{em}	CIPR	26,315±370	891±208	942±279	2,648±419	—	0.936
	ENRO	26,492±345	−408±203	−2,245±348	−2,482±362	—	0.947
ϕ_f	CIPR	0.019±0.060	0.099±0.033	0.167±0.0449	0.089±0.065	0.018±0.004	0.935
	ENRO	0.019±0.060	0.099±0.033	0.167±0.0449	0.089±0.065	0.018±0.004	0.935
ϕ_{f^*}	CIPR	−0.061±0.104	0.151±0.056	−0.122±0.0791	0.193±0.111	—	0.745
	ENRO	−0.146±0.058	0.134±0.034	−0.113±0.058	0.311±0.060	—	0.898

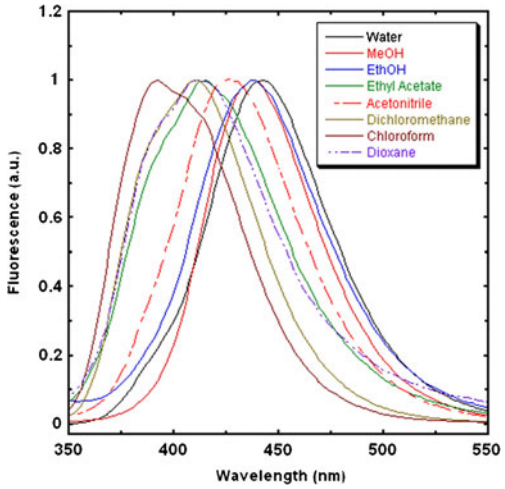

Fig. 2 Normalized fluorescence spectra of ENRO (5×10^{-6} M) in selected solvents; (λ_{ex}=275 nm)

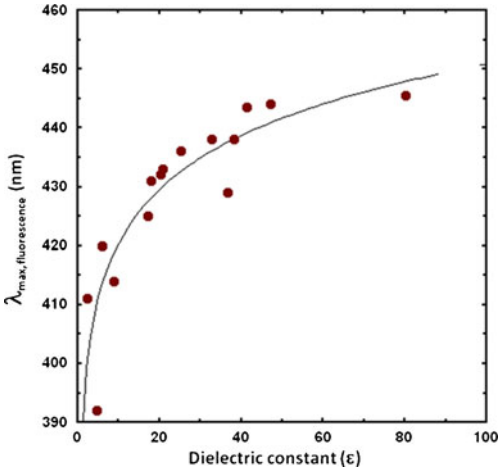

Fig. 4 Plot of variation of fluorescence maximum of ENRO (5×10^{-6} M) as a function of dielectric constant of different solvents (λ_{ex}=275 nm)

maxima (cm^{-1}) to the orientation polarizability, where the later is defined as [5]:

$$\Delta f = \frac{\varepsilon - 1}{2\varepsilon + 1} - \frac{n^2 - 1}{2n^2 + 1}$$

where n and ε are the solvent refractive index and solvent dielectric constant, respectively. Hence, the Δf relationship considers both the effect of solvents solvent electrons redistribution and dipoles reorientation and on the total polarity of the solvent; where, the first term $\left(\frac{\varepsilon-1}{2\varepsilon+1}\right)$ and second term $\left(\frac{n^2-1}{2n^2+1}\right)$ represent the contribution of a combination of solvent electrons redistribution and solvents dipoles reorientation, and the electrons redistribution effect only, respectively. According to Lippert-Mataga theory the orientation polarizability is correlated to the Stokes shift of a fluorophore as [5]:

$$Strokes\ Shift = \frac{2\left(\mu_g - \mu_e\right)^2}{hca^3}\Delta f + const.$$

where μ_g and μ_e are the dipole moments of the molecule in its ground and excited states, respectively; h: Planck's constant, α: the cavity radius in which the fluorophore resides, c: is speed of light. The Stokes shift obtained for both drugs in different solvents is plotted against orientation polarizability of the corresponding solvents as illustrated in Fig. 5 (ENRO). As Lippert-Mataga theory does not take into consideration the solvent ability for hydrogen bonding, hence biphasic behavior is expected. The solvents where subdivided into two groups, namely able and unable hydrogen bonding groups, where the linear correlation of Lippert-Mataga was applied separately into these two subgroups. The notable difference between the

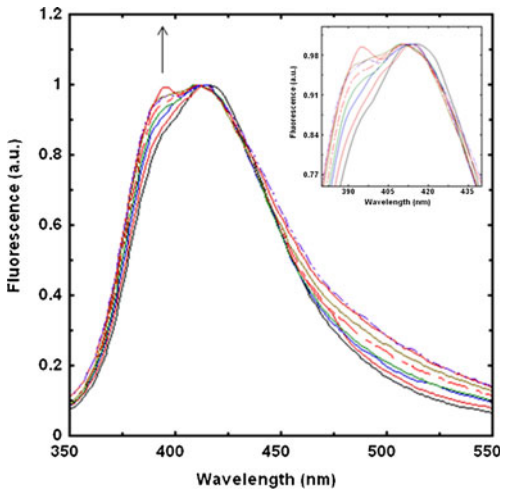

Fig. 3 Normalized fluorescence spectra of ENRO in dioxane with increasing level of hexane; the arrow indicates the direction of increase in the first band; inset: enlarged image for the same spectra at $\left(\lambda_{max}^{em}\right)$; λ_{ex}=280 nm

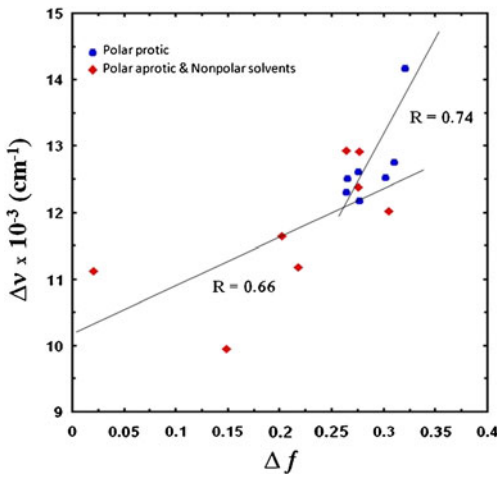

Fig. 5 The Lippert-Mataga plots (Stokes shift ($\Delta\nu$) vs. Δf) of ENRO (5×10^{-6} M) ; (λ_{ex}=275 nm)

two linear fittings implies that solvent influences the photophysicochemical properties of fluoroquinolones via two mechanisms, namely general and specific solvent effects, where these two kinds of effects can be concluded from the linear fittings of two subgroups of solvents, namely capable and incapable of hydrogen bonding solvents, respectively. These results signify the importance of hydrogen bonding in stabilizing or destabilizing the excited state of the selected fluoroquinolones. It is noteworthy mentioning that increasing solvent polarity did not only affect the position of λ_{max}^{em}, but also this change was accompanied by losing the structure of the fluorescence spectrum from double-band into single-band spectrum. Interestingly, this can potentially considered as an indication for the existence of two different excited states that result upon light absorption, i.e. emitting species, namely locally excited state (LE) and ICT state, which are observed in nonpolar and polar with solvents, respectively, where ICT for ENRO with higher charge separation is observed in more polar solvents. Proposed mechanisms for ICT of ENRO are illustrated in Fig. 6. Furthermore, the fluorescence and absorption spectra of ENRO were collected in binary solvent systems, namely dioxane-water binary system, where the dioxane v:v concentration varies in the range 0–100 %, see Fig. 7. Adding small volumes of water (5 %, v:v) has resulted in substantial bathochromic shift in the fluorescence spectrum of ENRO in dioxane ($\Delta\lambda \approx 20$), whereas almost no effect was observed in the absorption spectrum ($\Delta\lambda \approx 1$ nm) under the same conditions. Interestingly, it is noteworthy pointing out that the added volume of water is so small to alter the polarity of the medium, and hence this behavior can be attributed to the presence of specific solvent effect, hydrogen bonding in particular, that is consistent with those results obtained from Lippert plot. Similarly, the existence of general solvent effect was further evidenced from studying the effect of adding n-dioxane on the fluorescence spectrum of ENRO in chloroform or hexane, see Fig. 3. As can be noticed from Fig. 3, the resolution of the structured spectrum has dramatically enhanced with notable hypsochromic shift with increasing added volume of hexane implying the existence of the general solvent effect that is consistent with what was concluded from Lippert plot.

As listed in Tables 1 and 2, both λ_{max}^{abs} and λ_{max}^{em} for both drugs are affected by solvent polarity, and consequently the Stokes shift is also affected, which in turn indicates that the solvent interacts with both the ground and excited states of ENRO and CIPR. The μ_g and cavity radius (α) were estimated using molecular mechanics (MM+) calculation based on the most stable 3-D structure of the drug and were found to be equal to 5.8 Debye and 5.0 Å, respectively for ENRO and 5.7 Debye and 4.8 Å, respectively, for CIPR. $\Delta\mu$ for both the LE and ICT states were estimated from the linear regressions in the Lippert plot for hydrogen bonding able and unable subgroups of solvents, respectively, and found to be 16.2 and 9.4 Debye, respectively, for ENRO, and 16.2 and 8.0 Debye for CIPR. Hence, using the estimated values of $\Delta\mu$ in protic solvents, μ_g and α, μ_{ex} was calculated and found to be 22.0 and 23.0 Debye for ENRO and CIPR, respectively, which corresponds to average charge separation of approximately 4.6 Å, which in turn is comparable with the molecular size of the selected fluoroquinolones estimated using MM + calculation.

Effect of solvent polarity and viscosity on fluoroquinolones fluorescence quantum yield (Φ_f) was also investigated. As can be noticed from Table 1, Φ_f notably increases with increasing solvent polarity and viscosity, where similar results obtained from considering both effects indicating that the non-radiative decay decreases with increasing either one of them. In terms of polarity, the decrease in Φ_f as polarity decreases could be linked with the ICT, where the ICT is less stabilized in solvents of lower polarity and consequently free rotation is less retarded, and hence rate

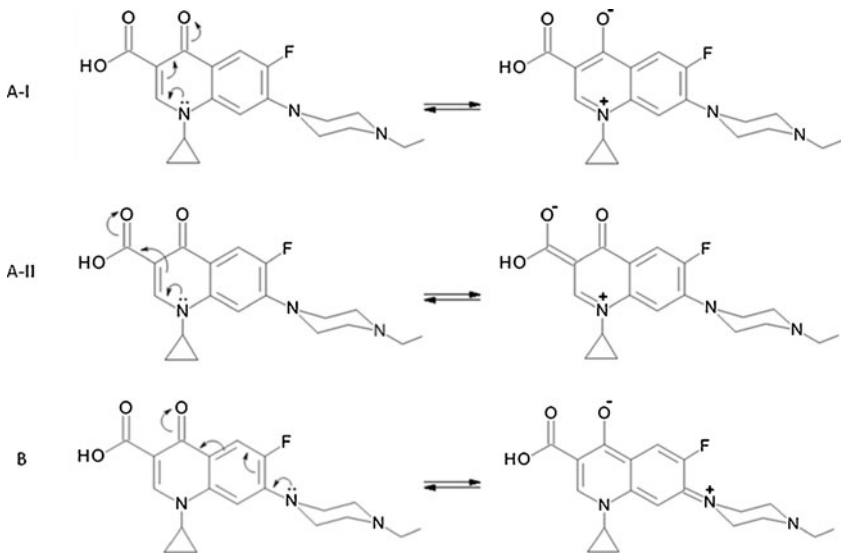

Fig. 6 Proposed ICT for ENRO

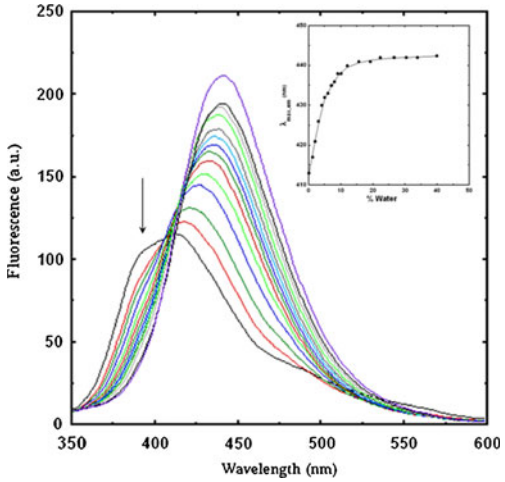

Fig. 7 fluorescence spectra of ENRO in dioxane with increasing level of water; the arrow indicates the direction of fading in the first band; inset: effect of solution composition on λ_{max}^{em} of ENRO; λ_{ex}=280 nm

of non-radiative decay increases, which in turn can be observed as a reduce in Φ_f. Similarly, increase in Φ_f as viscosity increases can be attributed to retardation of free rotation upon forming the ICT; such behavior can be obviously observed in viscous solvent, such as DMSO (Φ_f =0.12, Δf = 0.26) and ethylen glycol (Φ_f =0.28, Δf = 0.25), yet these two solvent possess lower polarizability than other solvents, such as methanol (Φ_f =0.02, Δf = 0.31) including all alcohols. However, it is noteworthy mentioning that it is more conclusive to consider dual effect of polarity and viscosity. Attempts were conducted for correlating either the solvent viscosity or polarity separately with the Φ_f of both drugs, where inconclusive correlation was observed. See below for more information.

Supporting the findings that were obtained using the Lippert-Mataga methodology was attempted via correlating the λ_{max}^{em} and Stokes shifts of selected fluoroquinolones with the normalized polarity parameter $E_T(30)$. Figure 8 shows the plots of Stokes shift (A) and λ_{max}^{em} (B) of ENRO as a function of E_T (30). It can be noticed that a weak correlation was obtained when all solvents were included in the correlation. Nevertheless, subdividing these solvents into the same subgroups, as performed in Lippert plot, revealed reasonable (R= 0.96) and weak correlation for the protic and aprotic subgroups of solvents, respectively, highlighting the importance of specific solvent effect on fluoroquinolones photophysicochemical properties. Alternatively, a new multiparameter approach that was developed by Kamlet et al. concerning correlating various solvents' parameters with measurable physicochemical property or parameter (XYZ) [26, 27], has exhibited notable successful physical interpretation and correlation for experimental data. The general form of Kamlet-Taft multiparameter correlation equation concerning solvatochromism is expressed as:

$$XYZ = XYZ_o + a\alpha + b\beta + c\pi^*$$

where, XYZ is the measurable physical parameter; XYZ_o is the measurable physical parameter in the gas phase, i.e. solvent independent physical parameter; a, b and c are solvents independent coefficients; α, β and π* are the hydrogen-bond donor capability, hydrogen-bond acceptor capability, and dielectric effects of solvents (polarizability), respectively. The multiple linear regression analysis (MLRA) was performed against several XYZ parameters, namely absorption frequency (ν_{abs}), emission frequency (ν_{em}), Stokes shift ($\Delta\nu$), and Φ_f. However, as mentioned earlier other factor that can contribute to the value of Φ_f is solvent viscosity, hence the Kamlet-Taft equation was modified in case of Φ_f by inserting the solvent viscosity (η):

$$\Phi_f = \Phi_{f_o} + a\alpha + b\beta + c\pi^* + d\eta$$

Estimated values for the solvent independent coefficients, standard deviation, and correlation coefficient (R) obtained from applying the MLRA are summarized in Table 2. Interestingly, the relatively high correlation coefficients obtained for all XYZ of interests (R: 0.916–0.966) implies that the experimental data are highly linearly correlated, where this excellent correlation was obtained without separating tested solvents into subgroups. The MLRA that corresponds Φ_f

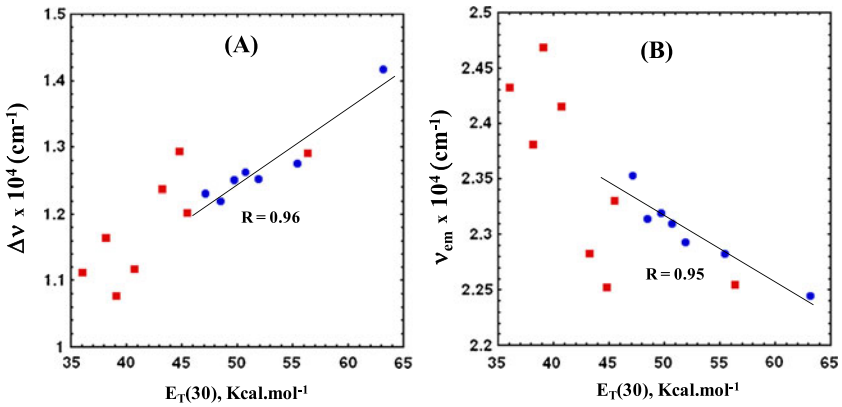

Fig. 8 Plot of Stokes shift (**a**) and ν_{em} of ENRO (5×10^{-6} M) vs. $E_T(30)$ of different solvents (λ_{ex}=275 nm)

was performed twice, with and without taking into consideration the solvent viscosity effect, (Φ_f) and (Φ_{f*}), respectively; no significant enhancement was observed upon taking into consideration the viscosity factor. The closeness of obtained values for the corresponding correlation coefficients (R (Φ_f)=0.898; R (Φ_{f*})=0.916) implies that solvent viscosity contributes minorly to the Φ_f of the selected fluoroquinolones in comparison to other factors, but cannot be completely disregarded. Furthermore, it can be noticed from Table 2 that solvents polarizability contributes majorly in all XYZ, but it can be noticed too that hydrogen bonding also has significant contribution. MLRA was also performed against ν_{abs} (data not shown), however inconclusive results were obtained due to the corresponding unsatisfactory correlation coefficient (R=0.63). Indeed, the data in Table 2 show that both solvent polarizability and hydrogen-bond acceptor ability contribute positively to the Stokes shift and emission frequency, which implies stabilization of the corresponding state. On the other hand, hydrogen-bond donor ability contributes positively (stabilization) and negatively (destabilization) to Stokes shift and emission frequency, respectively, where such contradictory contribution can be attributed to the fact that it is generally impractical to investigate the effect of solvent polarity on emission frequency separately from the absorption frequency. Hence, this consistently with other results that solvent does affect both the ground and excited states of the selected fluoroquinolones.

Conclusion

The solvent-dependent photophysicochemical properties of selected fluoroquinolones have been successfully investigated using steady state fluorescence techniques. Solvents of different physical properties including solvation parameters, such as normalized polarity parameter ($E_T(30)$), dipolarity/polarizability (π^*), hydrogen-bond donor acidity (α), and hydrogen-bond acceptor basicity (β), were used successfully for the purpose of gaining insights concerning the influence of solvent on the photophysicochemical properties of fluoroquinolones drugs. Obtained results indicated that fluorescence spectra of ENRO and CIPR are notably influenced by the solvent polarity and its hydrogen bonding ability. This report demonstrates that this solvent dependant fluorescence behavior of both drugs can be utilized for gaining insights concerning its excited state behavior. In particular, two emitting species for the selected drugs, namely locally excited state (LE) and intramolecular charge transfer (ICT) state may exist upon excitation of ENRO, where these two states correspond to the excited states that are generated in aprotic and protic solvents, respectively. Interestingly, consistent results were obtained upon applying different correlating techniques against the experimental data, namely Lippert-Mataga and Kamlet-Taft techniques. The findings of this study can be employed for gaining conclusive knowledge concerning the phototoxicity of this drug and other structurally related drugs under similar biological environments in terms of polarity and viscosity. .

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