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Fate of anticancer drug ellipticine in reverse micelles in aqueous and methanolic environment: A photophysical approach

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ABSTRACT

The present investigation explored a detailed photophysics of an anticancer agent ellipticine, in AOT reverse micelle using steady state and time resolved spectroscopy. We observed that ellipticines are entrapped as a cationic species in AOT/hexane system. Increase in water content in reverse micelles, entraps more number of cationic species while increase in methanol content causes switch over of cationic ellipticine to a neutral species. Unlike in pure methanol, we did not observe any solvent assisted proton transfer in AOT/hexane/methanol system. This unique observation was explained by the inhomogeneity of methanol entrapped in AOT/hexane system.

1. Introduction

Ellipticine is a pyridocarbazole type plant alkaloid which exhibits cytotoxic activity against tumor cells. Methoxy ellipticine lactate and 2-methyl-9-hydroxyl ellipticinium acetate exhibit a significant biological activity [1]. The biological action of these pyridocarbazoles results in direct binding to DNA [2–7]. They induce protein associated DNA strand break by trapping Topoisomerase II [3–11].

Recently, ellipticine has attracted a number of scientists to investigate its photophysics in different solvents. In nonpolar solvent like hexane, ellipticine exhibits absorbance and emission maxima at 364 and 385 nm respectively [12]. The lifetime was reported around 15 ns [12]. In moderately polar solvents like dimethyl sulfoxide (DMSO) and dimethyl formamide (DMF) the emission takes place at around 425 nm with lifetime constant around 27 ns [12]. The long lifetime was attributed to strong hydrogen bonding between the charge transfer state of ellipticine and DMSO and DMF [12]. In methanol, ellipticine exhibits a dual emission at 435 and 535 nm. Miskolczy et al. attributed the long wavelength fluorescence band (535 nm) to the excited state proton transfer reaction by the solvent [13,14]. The rate of protonation in the excited state was reported to be $9.8 \times 10^7\ s^{-1}$. On the other hand, Banerjee et al. attributed the longer wavelength emission in methanol to the solvent assisted tautomerization from pyrol ring to pyridine ring. This report is in accordance with that reported by Cabo et al. [15]. The study of Banerjee et al. [16] suggests that excited state reaction involves solvent reorganization around ellipticine to form 'cyclic' solvated species which facilitates a rapid proton transfer and the two emission bands arise from the normal and tautomeric form. This is well established by excitation spectra of methanol and time resolved studies.

It has already been reported that ellipticine exists as protonated or deprotonated species in aqueous medium [17–22]. The major shortcomings in usage of neutral ellipticine as a pharmaceutical are its toxicity and low solubility in water, but cationic species, ellipticinium is more soluble in water than neutral ellipticine [20]. We can overcome the problem of low solubility of ellipticine in aqueous media by attaching the drug to polymer, peptide or micelle [23,24]. Ellipticine and its 9-methoxy analog have a net amphiphatic character, which gives ability to interact with the membrane [25]. Thus detailed knowledge of physical and chemical properties is necessary. In this context, reverse micelles (RM) provide an attractive model for bio-systems since they can mimic several important and essential features of biological membranes. The motivation of photophysical study of ellipticine in reverse micelles comes from its role as photosensitizer of DNA clevage [26]. It is already reported that in cytoplasm ellipticine exists in both neutral and protonated forms but in nucleus it exist as only protonated species [27]. Study of photophysical properties inside RM and its switchover from one species to another species will certainly help to understand the photophyscial behavior of ellipticine inside biological membrane and its role as photosensitizer trigger of nuclease activity inside tumor cell. One of the significant features of RMs is the presence of highly structured and nonhomogeneous water molecules, which represents an interesting model of water molecules present in biological systems such as membranes [24–30]. Enzyme-containing RMs may offer novel tools for biotechnology and for drug delivery through solubilization of lipophilic drugs [31]. Ellipticine forms a stable complex with Topoisomerase II [3–11]. In our previous effort, we studied the interaction of ellipticine in liposome environments [32]. From the viewpoint of future biophysical applications, it is necessary to make a vivid study of

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the photophysical processes of ellipticine in Aerosol-OT (AOT) reverse micelles.

2. Experimental

Sodium bis(2-ethylhexyl)sulfosuccinate (AOT) and hexane were purchased from Aldrich and were used without further purification. AOT was dried for 48 hours before use. Spectroscopic grade methanol from Merck and HPLC grade water from Rankem, India were used as received. We express water content (w_0) and methanol content (w_m) inside the reverse micelles using the following equation:

$$w_s = \frac{[\text{solvent}]}{[\text{AOT}]}$$

In a recent publication, Levinger et al. defined AOT/hexane/methanol system as a microemulsion, as this is a continuous system [33]. However, in this manuscript we would prefer the inhomogeneity of methanol in AOT/hexane/methanol system as reported by other groups [34–36].

Steady state absorption spectra were taken in a Varian UV–Vis spectrometer (Model: Cary 100). Emission spectra were taken in a Fluoromax-4p fluorimeter from Horiba Jobin Yvon (Model: FM-100). The samples were excited at 375 nm. All the measurements were done at 25 °C.

For the time resolved studies, we used a picosecond time correlated single photon counting (TCSPC) system from IBH (Model: Fluorocube-01-NL). The experimental setup for TCSPC has been described elsewhere [32]. The samples were excited at 375 nm using a picosecond diode laser (Model: Pico Brite-375L). The signals were collected at magic angle (54.70°) polarization using a photomultiplier tube (TBX-07C) as detector. The instrument response function of our setup is ~140 ps.

The amplitude weighted average lifetime was calculated using following equation

$$\langle \tau \rangle = \sum_{i=1}^{n} a_i \tau_i \quad (1)$$

where τ_i are the fluorescence lifetimes of various fluorescent components and a_i are the normalized pre-exponential factors. We used the same setup for anisotropy measurements. The time resolved anisotropy was described with the following equation:

$$r(t) = r_0 \sum_{i=1}^{n} a_{ri} \exp\left(-\frac{t}{\tau_{ri}}\right) \quad (2)$$

where $r(t)$ is the rotational relaxation correlation function. r_0 is the limiting anisotropy and τ_{ri} is the individual rotational relaxation time and a_{ri} is the normalized amplitude of rotational relaxation time.

3. Results

3.1. Steady state absorption and emission spectra

We took absorption and emission spectra in aqueous medium at different pH. Since the solubility of ellipticine is very less in aqueous medium (<10^{-6} M), so; absorption spectra particularly at longer wavelength is difficult of perception. Therefore, we would focus on excitation spectra of ellipticine in aqueous solution rather than absorption spectra. The emission spectra of ellipticine reveal that in acidic condition (pH ~ 2) the emission maximum takes place at 535 nm. On the other hand at pH 12, an additional band appears around 450 nm along with 535 nm band (Figure 1a). The excitation spectra at pH ~ 2 and pH ~ 12 were monitored at 535 and 450 nm, respectively (Figure 1b).

In hexane, the absorption band of ellipticine takes place at 364 nm. Addition of 0.1 M AOT to *n*-hexane produces two major absorption bands at 352 and 425 nm. The absorbance increases further with increase in w_0 value at 352 and 425 nm bands (Figure 2a). Surprisingly, we observe a reverse trend i.e. absorbance decreases with increase in w_m values at 425 nm wavelength in AOT/hexane/methanol system. Interestingly, two isobestic points appear at 297 and 409 nm which imply that more than one kind of species exist in the ground state in AOT/hexane/methanol system (Figure 2b).

The emission maximum of ellipticine in n-hexane appears at 385 nm. Addition of 0.1 M AOT to this solution shifts the emission band to 500 nm. The quantum yield increases from 0.15 to 0.28. With increase in the w_0 values, the emission spectra are found to be red shifted followed by a decrease in the quantum yield (Figure 3a). Addition of methanol to AOT/hexane system diminishes the intensity at 500 nm band while another emission band grows up at 442 nm. Surprisingly, at highest methanol content the emission band at 500 nm almost disappears and the emission band at the shorter wavelength (442 nm) becomes the primary band. We also observe an isoemissive point at around 466 nm (Figure 3b).

3.2. Time resolved studies

We measured fluorescence lifetime of ellipticine in aqueous medium at different pH. At pH ~ 10, the lifetime of ellipticine is bi-exponential and the time components are 0.182 ns (95%) and 5.6 ns (5%). At pH ~ 12 the lifetime is almost single exponential with a component of around 180 ps. At pH ~ 7, the lifetime is tri-exponential and consists the components of 0.182 ns (16%), 2.0 ns (80%) and 5.55 ns (4%). The lifetime did not change on going from pH ~ 7 to pH ~ 2.

In hexane the lifetime of ellipticine was reported earlier [12]. We took time resolved decays at 505 nm varying w_0 and w_m values. At w_0 = 0, the average lifetime is around 22 ns. The components are 1.10 ns (14%) and 25.35 ns (86%). The results are summarized in Table 1. On increasing w_0 values, longer component decreases and at highest water content (w_0 = 32) it becomes 9 ns (65%) while the shorter component decreases from 1 ns to 0.459 ns (35%). In AOT/hexane/methanol system, at highest methanol content (at w_m = 16) the longer component decreases to 11.23 ns (80%) and the shorter component is reduced to 0.606 ns (20%). The lifetime components are shown in Figure 4a and b, respectively.

We took time resolved anisotropy decays in hexane at 410 nm and in AOT/hexane system at 505 nm varying w_0 (Figure 5a) and w_m values (Figure 5b). In pure hexane, ellipticine exhibits a single exponential decay with time constant 145 ps. In AOT/hexane, the anisotropy decay becomes bi-exponential with the shorter (τ_{r1}) and longer (τ_{r2}) time constants of 1.00 and 2.93 ns, respectively (Table 2). The average rotational relaxation time decreases beyond w_0 = 4. Interestingly, decrease in rotational relaxation is massive in AOT/hexane/methanol system. Table 2 reveals that addition of methanol enormously enhances the amplitude of fast component from 27% to 81% at w_0 = 2. At w_m = 16, fast component dominates and anisotropy decay becomes almost single exponential (Figure 5b).

4. Discussions

Ellipticine has pK_a value around 7.40 in aqueous medium [37]. So; in aqueous medium ellipticine may exist as a protonated and deprotonated species depending on the pH of the medium [20–22] (Scheme 1). The protonation takes place at the nitrogen of

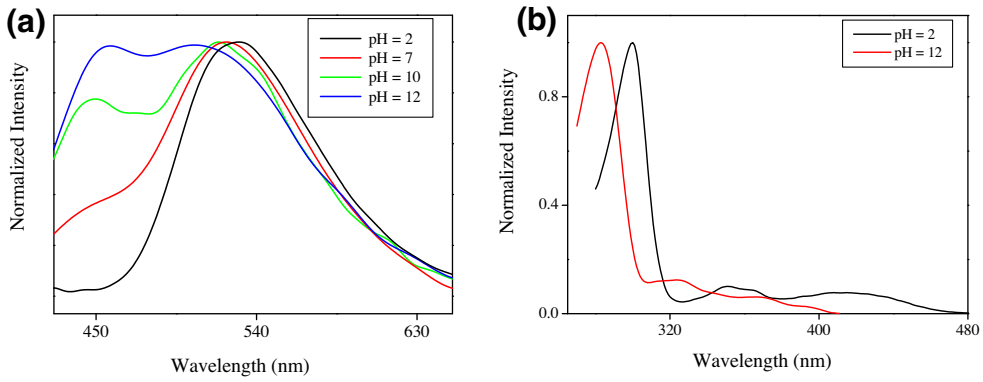


Figure 1. (a) Normalized emission spectra of ellipticine at different pH. (b) Normalized excitation spectra of ellipticine monitored at 535 nm at pH 2 and monitored at 450 nm at pH 12.

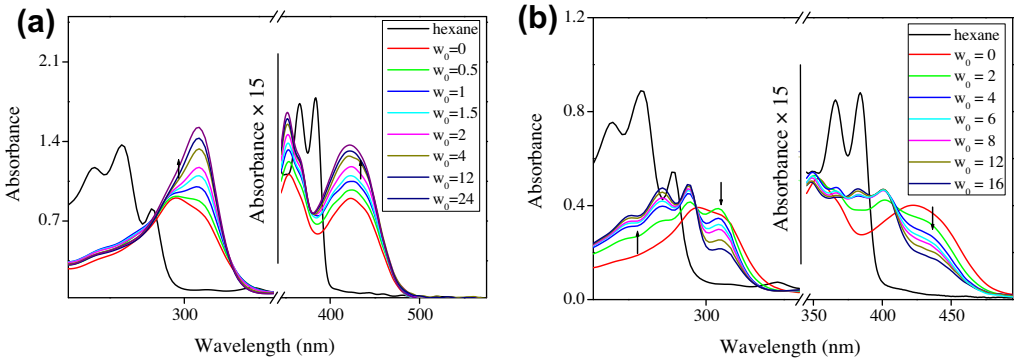


Figure 2. Absorption spectra of ellipticine in (a) *n*-Hexane and in aqueous reverse micelles at different w_0 values (0–32). (b) *n*-Hexane and AOT/hexane/methanol system at different w_m values (0–16).

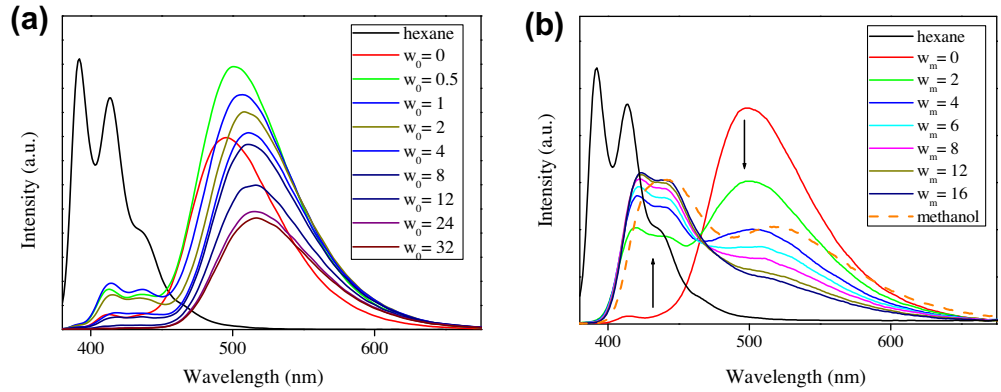


Figure 3. (a) The emission spectra of ellipticine in aqueous reverse micelles at different w_0 values. (b) The emission spectra of ellipticine in AOT/hexane/methanol system at different w_m values are shown. The dotted line indicates the emission of ellipticine in pure methanol, which is normalized at 442 nm with respect to maximum w_m value.

the pyridine ring. At pH ~ 7.0, ellipticine exhibits emission maximum at 535 nm which corresponds to the cationic species of ellipticine. We do not discard the possibility of excited state protonation as significant fluorescence intensity is observed at 535 nm at pH ~ 12. The excited state pK_a as deduced using Foster cycle is around 8.90 which indicates that excited state protonation is possible. However, the excitation spectra monitored at 535 nm at pH ~ 2 reveals a band at 425 nm which is almost similar to the absorption band of ellipticine in presence of trifluoroacetic acid in methanol [14]. Interestingly, the excitation spectra monitored at 450 nm pH ~ 12 reveals an absorption band at 350 nm which corresponds to a neutral species. This observation implies that ground state protonated species in aqueous medium are responsible for the observed emission band at 535 nm. We found that the quantum yield of cationic ellipticine (0.002) is several folds higher compared to that of its neutral species (0.0002). Thus a little amount of cationic ellipticine is enough to exhibit significant fluorescence intensity at 512 nm in basic medium (pH ~ 12).

With addition of AOT to hexane solution of ellipticine the absorption band appears at 425 nm which is quite similar to the absorption band of ellipticine in presence of trifluoroacetic acid in methanol [14]. In the latter system, ellipticine remains as cationic species in the ground state. Therefore, a similar absorption band suggests that the ellipticine molecules are entrapped as a cat-

Table 1
Lifetime components of ellipticine in AOT/hexane system as function of water (w_0) and methanol (w_m) contents at 505 nm.[a]

AOT/hexane	a_1 (%)	a_2 (%)	τ_1 (ns)	τ_2 (ns)	$\langle\tau\rangle$ (ns)	χ^2
$w_0 = 0$	0.14	0.86	1.1	25.35	22	1.07
$w_0 = 0.5$	0.17	0.83	1.20	22.50	19.25	1.15
$w_0 = 1$	0.20	0.80	1.40	21.50	17.50	1.10
$w_0 = 2$	0.27	0.73	1.63	18.37	13.89	1.16
$w_0 = 4$	0.31	0.69	0.91	16.03	11.32	1.17
$w_0 = 6$	0.34	0.66	0.624	14.21	9.65	1.17
$w_0 = 8$	0.34	0.66	0.546	12.99	8.77	1.14
$w_0 = 12$	0.36	0.64	0.491	11.548	7.589	1.21
$w_0 = 16$	0.35	0.65	0.488	10.76	7.174	1.21
$w_0 = 24$	0.36	0.64	0.438	9.886	6.47	1.19
$w_0 = 32$	0.35	0.65	0.459	9.479	6.33	1.15
$w_m = 0$	0.14	0.86	1.34	25.57	22.53	1.07
$w_m = 1$	0.13	0.87	1.60	20.00	17.60	1.10
$w_m = 2$	0.15	0.85	2.228	17.69	15.38	1.16
$w_m = 4$	0.17	0.83	1.79	13.96	11.94	1.17
$w_m = 6$	0.18	0.82	1.27	12.55	10.517	1.17
$w_m = 8$	0.20	0.80	1.04	11.86	9.74	1.14
$w_m = 12$	0.20	0.80	0.8169	11.36	9.213	1.21
$w_m = 16$	0.20	0.80	0.606	11.23	9.102	1.07

[a] Error in the measurement is around 5%.

Table 2
Rotational relaxation parameters of ellipticine in AOT/hexane system as function of water (w_0) and methanol contents (w_m) at 505 nm.[a]

AOT/hexane	a_{1r} (%)	a_{2r} (%)	τ_{1r} (ns)	τ_{2r} (ns)	$\langle\tau_r\rangle$ (ns)	r_0
$w_0 = 0$	0.28	0.72	1.00	2.93	2.39	0.27
$w_0 = 2$	0.34	0.66	1.40	3.00	2.456	0.32
$w_0 = 4$	0.42	0.58	1.20	3.20	2.389	0.32
$w_0 = 6$	0.42	0.58	0.763	3.28	2.222	0.32
$w_0 = 8$	0.50	0.50	.891	3.05	1.949	0.32
$w_0 = 12$	0.54	0.46	0.882	3.126	1.924	0.32
$w_0 = 16$	0.62	0.38	0.738	3.00	1.564	0.29
$w_0 = 32$	0.58	0.42	0.644	2.44	1.424	0.30
$w_m = 0$	0.27	0.73	1.23	2.98	2.503	0.27
$w_m = 2$	0.81	0.19	1.126	2.553	1.395	0.32
$w_m = 4$	0.87	0.13	0.705	2.693	0.948	0.34
$w_m = 6$	0.86	0.14	0.464	2.527	0.755	0.29
$w_m = 12$	0.90	0.10	0.300	1.450	0.483	0.26
$w_m = 16$	1	–	0.367	–	0.367	0.25

[a] Error in the measurement is around 5%.

ionic species in AOT/hexane system. The increase in absorbance at 425 nm with increase in w_0 confirms that neutral ellipticine are converted into the cationic species. This conjecture is also supported by a huge red shift (from 385 to 505 nm) in the emission spectra with addition of AOT to hexane solution and subsequent red shift with increase in w_0 values. The lack of isoemissive point indicates that single kind of species exists in aqueous reverse micelles and this species is ellipticinium cation. However, in AOT/hexane/methanol system, we observed a reverse trend in absorption and emission spectra. The decrease in absorbance at 425 nm band with increase in w_m values corroborates well with the mechanism that cationic species are converted into the neutral species. This switchover is well supported by the appearance of emission band at 442 nm and subsequent decrease in the intensity at longer wavelength (505 nm) band. The appearance of isobestic points at 409 nm and isoemissive point at 466 nm indicates that more than one species exist in the system. The switchover of neutral ellipticine into cationic in aqueous reverse micelles and vice versa in

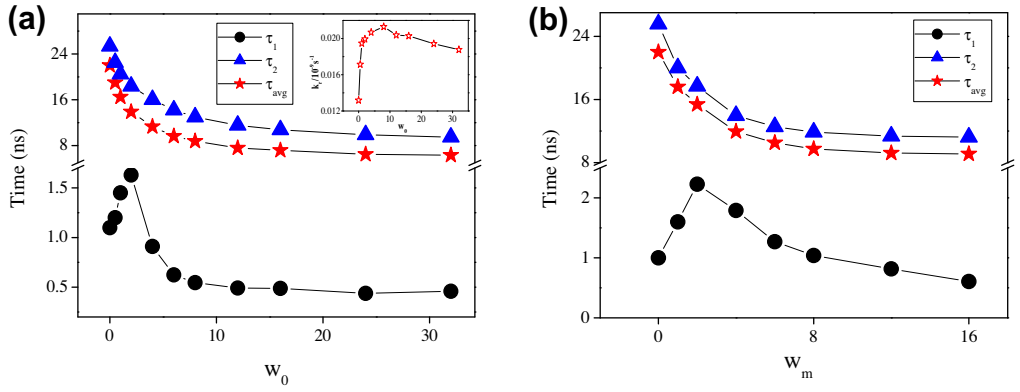


Figure 4. The lifetime components τ_1, τ_2 and τ_{avg} of ellipticine (a) at different w_0 values. In the inset the variation of radiative rate constant (k_r) at different w_0 values are shown. (b) The same at different w_m values.

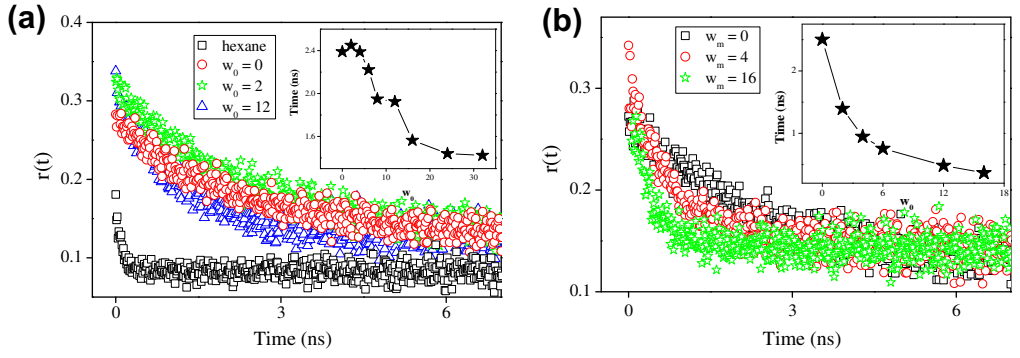
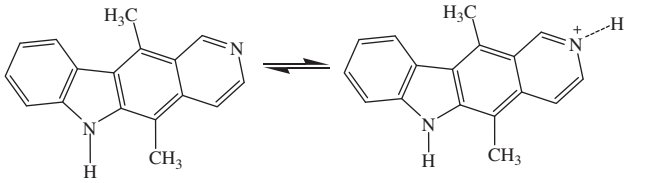
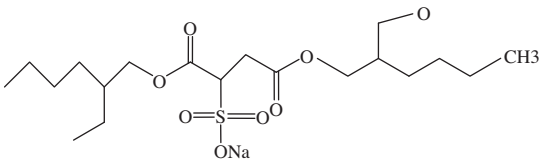


Figure 5. Fluorescence anisotropy decays of ellipticine in (a) aqueous reverse micelles at different w_0 values. In the inset the rotational relaxation time at different water content is shown. (b) AOT/hexane/methanol system at different w_m values. In the inset the rotational relaxation time at different methanol content is shown.



Prototropic form of ellipticine



AOT

Scheme 1.

AOT/hexane/methanol system can be explained if one considers the structural inhomogeneity of water and methanol in AOT/hexane systems [34–36]. It has been previously reported [38,39] that the pH of water molecules associated with sulfonate groups in the nanocavity of AOT reverse micelles is less than the bulk pH, as hydronium ions of water are attracted to the negatively charged sulfonate group. The increased local acidity causes the protonation of the ellipticine in the interfacial region and the cations are stabilized by the negatively charged interface. Thus in aqueous reverse micelles more number of ellipticine molecules are converted into cationic species and migrate to water pool which is followed by a continuous red shift and decrease in the intensity. A similar kind of ground state protonation of 2,2′pidyl) benzimidazole in aqueous reverse micelles has been reported by Mukherjee et al. [38]. Unlike ground state protonation with increase in w_0 values, a different picture is observed with increase in w_m values. It has been reported that with increase in w_m values, sulfonate bound methanol molecules increase significantly but bulk type methanol remains constant [34–36]. Venables et al. [35] reported long back that methanol molecules that are hydrogen bonded to the head groups of the surfactant cannot donate hydrogen bonds to other methanol molecules and the methyl groups would be directed towards the center of the reverse micelles, resulting in considerable steric congestion. Setua et al. [34] reported that with increasing w_m, the area fraction of the bulk methanol remains practically constant. Therefore, in the present study, with increase in w_m values two phenomena take place. The first one is the switch over of cationic ellipticinium ions to the neutral species and the second one is that the removed ellipticines do not undergo any solvent assisted proton transfer reaction. This is because of the fact that in AOT interface the methanol molecules are strongly bound to the AOT head groups and these sulfonate bound molecules do not have any extensive hydrogen bonding network.

The ground state protonation of ellipticine corroborates well with the lifetime data of ellipticine in aqueous solution and in AOT reverse micelles. We already assigned that in aqueous solution the picosecond component originates from the neutral species and nanosecond component originates from the cationic species. The increase in the picosecond component from 16% to 95% and subsequent decrease in the nanosecond component upon change in pH from pH $\sim$ 2 to pH $\sim$ 10 clearly indicate that the emission property is dominated by the cationic species at lower pH and has a longer lifetime than neutral species. In AOT/hexane solution the longer lifetime is around 25.35 ns (86%) which is 12 times more than that in aqueous solution. The huge increase in slow component results from the strong electrostatic interaction between cationic ellipticine and negatively charged head group of AOT. Therefore, neutral species that are bound to the interfacial region are responsible for shorter component of 1 ns (14%). It is important to note that with increase in w_0 values the fast component decreases from nanosecond to picosecond component. The decrement in the fast component from the nanosecond to picosecond indicates that at larger water content, ellipticine molecules experience environment similar to that in aqueous medium. Interestingly, it is observed that till $w_0 = 2$ the shorter component increases from 1.10 to 1.60 ns. This could be due to the fact that initially with increase in water content, the hydrophobic neutral ellipticine may be pushed to more confined region. This fact results in an increase in the shorter lifetime. The bound water molecules in the interfacial region may form a tight bonding with neutral ellipticine through hydrogen bonding. The binding between the bound water molecules (bound to AOT head group) and ellipticine may lead to an increase in shorter component. However, in AOT/hexane/methanol system, the cationic ellipticines switch over to neutral species and are removed from the electrostatic attachment with the AOT head groups. This fact reduces the shorter and longer component in AOT/hexane/methanol system. It has been reported earlier by Banerjee et al. [12] that ellipticine undergoes a solvent assisted proton transfer in methanol. We measured lifetime at 560 nm in AOT/hydrocarbon/methanol system. However, we did not observe any rise component even at highest methanol content. This fact also indicates that in reverse micelles bulk methanol does not increase with increase in w_m.

The interaction between the cationic ellipticine and AOT reverse micelles is also probed by anisotropy data. The bi-exponential decay of ellipticine in AOT/hexane system with nanoseconds components indicates that ellipticines are entrapped inside the reverse micelles. Table 1 reveals that with increase in w_0 values, the anisotropy increases till $w_0 = 4$. The r_0 value increases from 0.27 to 0.32. Ellipticine being very hydrophobic in nature is unlikely to penetrate deep inside the reverse micellar pool. The cationic species of ellipticine prefer to bind to the negatively charged head groups of AOT. Table 1 reveals that the longer time constant (τ_{r2}) remains same with increasing w_0, till $w_0 = 16$. We, therefore, ascribe the slower motion to be originating from the strong coupling between anionic head group of AOT and cationic ellipticine and this is independent till $w_0 = 12$. The shorter component (τ_{r1}) may originate from those species which remain unbound in the interfacial region. The decrease in the time constant of shorter component from 1 ns to 0.644 ns and subsequent increase in its amplitude from 28% to 58% indicate that at higher w_0, a few ellipticine molecules penetrate inside the reverse micelles leaving AOT interfacial region. On the other hand in AOT/hexane/methanol system at highest w_m value, the fast component only dominates and anisotropy becomes almost single exponential. We already mentioned that with addition of methanol to AOT/hexane system, cationic ellipticinium ions are converted into the neutral species. As the bulk methanol does not increase with w_m values, so; the ellipticine molecules which are removed from the interfacial region will remain unbound because methanol is single hydrogen bond donor and being bound to sulfonate group cannot offer any additional hydrogen bond towards ellipticine.

5. Conclusion

The present study reveals that ellipticine molecules are entrapped as a cationic species in AOT/hexane system with increase in w_0 values while with increase in the w_m values, cationic ellipticine is converted into neutral species. Interestingly, even at highest methanol content, we did not observe any solvent assisted proton transfer. We attribute this fact to the lack of bulk methanol in an

AOT/hexane/methanol system. Moreover, methanol mostly binds to AOT head group region. Therefore, these methanol molecules are unable to donate a proton to ellipticine as well as do not facilitate solvent assisted proton transfer. This fact is responsible for the observed decrease in fluorescence at longer wavelength in AOT/hexane/methanol system.

Acknowledgments

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References

[1] G.W. Gribble, The Alkaloid Chemistry and Pharmacology, Academic Press, San Diego, CA, 1990.
[2] C.L. Arteaga, D.L. Kisner, A. Goodman, D.D. Ven, Eur. J. Cancer Clin. Oncol. 23 (1987) 1621.
[3] N.C. Garbett, D.E. Graves, Curr. Med. Chem. 4 (2004) 149.
[4] A.F. Smith, E.C. Horning, S. Goodwin, J. Am. Chem. Soc. 81 (1959) 1903.
[5] J.-B. Le Pecq, N.-D. Xuong, C. Gosse, C. Paoletti, Proc. Natl. Acad. Sci. USA 71 (1974) 5078.
[6] L. Larue, C. Rivalle, G. Muzard, C. Paoletti, E. Bisagni, J. Paoletti, J. Med. Chem. 31 (1988) 1951.
[7] K.W. Kohn, M.J. Waring, D. Glaubiger, C.A. Friedman, Cancer Res. 35 (1975) 71.
[8] M. Ohashi, T. Oki, Expert Opin. Ther. Pat. 6 (1996) 1258.
[9] R.B. Woodward, G.A. Iacobucci, F.A. Hochstein, J. Am. Chem. Soc. 81 (1959) 44349.
[10] C. Paoletti, C. Lesca, S. Cros, C. Malvy, C. Auclair, Biochem. Pharmacol. 28 (1979) 345.
[11] L.A. Zwelling, S. Michales, D. Kerrigan, Y. Pommier, K.W. Kohn, Biochem. Pharmacol. 31 (1982) 3261.
[12] S.Y. Fung, J. Duhamel, P. Chen, J. Phys. Chem. A 110 (2006) 11446.
[13] Z. Miskolezy, L. Biczok, J. Photochem. Photobiol. A 182 (2006) 82.
[14] Z. Miskolczy, L. Biczok, I. Jablonkai, Chem. Phys. Lett. 427 (2006) 76.
[15] J.L. Cabo, H.B. Faria, S.G.M. Portuga, M.A.A. Silva, I.M. Brinn, Photochem. Photobiol. 69 (1999) 664.
[16] S. Banerjee, A. Pabbathi, M. Chandra Sekhar, A. Samanta, J. Phys. Chem. A 115 (2011) 9217.
[17] S. Goodwin, A.F. Smith, E.C. Horning, J. Am. Chem. Soc. 81 (1958) 1903.
[18] S. Cros, R. Sorbara, C. Moisand, N.D. Xuong, P. Lecointe, C. Paoletti, Toxicol. Appl. Pharmacol. 33 (1975) 969.
[19] M. Sbai, S.A. Lyazidi, D.A. Lerner, B. del Castillo, M.A. Martin, Anal. Chim. Acta 303 (1995) 47.
[20] M. Schwaller, B. Allard, J. Phys. Chem. 98 (1994) 4209.
[21] J.M. El Hage Chahine, J.-P. Bertigny, M.-A. Schwaller, J. Chem. Soc. Perkin Trans. 2 (1989) 629.
[22] M. Sbai, S.A. Lyazidi, D.A. Lerner, B. del Castillo, M.A. Martin, Analyst 121 (1996) 1561.
[23] S. Fung, H. Yang, P.T. Bhola, P. Sadatmousavi, E. Muzar, M. Liu, P. Chen, Adv. Funct. Mater. 18 (2008) 1.
[24] J. Liu, Y. Xiao, C. Allen, J. Pharm. Sci. 93 (2004) 132.
[25] E.M. El Mashak, C. Paoletti, J.F. Tocanne, FEBS Lett. 107 (1980) 155.
[26] L. Perrouault et al., Nature 344 (1990) 358.
[27] M.A. Schwaller, B. Allard, J. Phys. Chem. 98 (1994) 4209.
[28] K. Bhattacharyya, B. Bagchi, Chem. Rev. 100 (2000) 20460.
[29] K. Bhattacharyya, B. Bagchi, J. Phys. Chem. A 104 (2000) 10603.
[30] D. Bose, D. Sarkar, A. Girigoswami, A. Mahata, D. Ghosh, N. Chattopadhyay, J. Chem. Phys. 131 (2009) 114707.
[31] R. Biswas, S.K. Pal, Chem. Phys. Lett. 387 (2004) 221.
[32] R. Thakur, A. Das, A. Chakraborty, Phys. Chem. Chem. Phys. 14 (2012) 15369.
[33] N.M. Correa, J.J. Silber, R.E. Riter, N.E. Levinger, Chem. Rev. 112 (2012) 4569.
[34] P. Setua, D. Seth, N. Sarkar, Phys. Chem. Chem. Phys. 11 (2009) 8913.
[35] D.S. Venables, K. Huang, C.A. Schmuttenmaer, J. Phys. Chem. B 105 (2001) 9132.
[36] P. Hazra, D. Chakrabarty, N. Sarkar, Langmuir 18 (2002) 7872.
[37] S.J.F. Amman, W.P. Marcia, N. Osheroff, R.B. Thompson, J. Biol. Chem. 270 (1995) 14998.
[38] T.K. Mukherjee, D. Panda, A. Datta, J. Phys. Chem. B 109 (2005) 18895.
[39] S.K. Pal, D. Mandal, K. Bhattacharyya, J. Phys. Chem. B 102 (1998) 11017.