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Photo-physical behavior of some antitumor anthracycline in solvent media with different polarity

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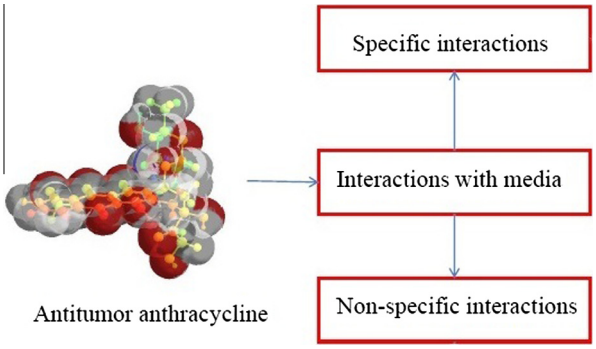
HIGHLIGHTS

- Self-aggregation of aglycone moiety show main change in solvatochromism of anthracycline.
- Intramolecular charge-transfer takes place in all three anthracycline samples.
- Reorientation of doxorubicin and epirubicin molecular functions in polar environment increases.
- Idarubicin's functional groups reorientation increases in hydrogen bond donor media.

GRAPHICAL ABSTRACT



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ABSTRACT

Absorption and emission spectra of three antitumour anthracyclines, with various substituent and stereoisomer groups, were studied in different solvents. The solute's photo-physical behavior strongly depends on solvent–solute interactions and solvent's nature. Solvatochromic method was used to investigate dipole moments of these materials in ground and excited states. Spectral variations were analyzed via means of linear solvation energy relationships concept, proposed by Kamlet and Taft. The results explain the nature of specific and non-specific solvent–solute interactions and functional groups' reorientation of studied anthracyclines in different media.

Introduction

Anthraquinones (AQ) are one of the largest and most important classes of organic compounds in nature [1]. Anthraquinones derivatives have several industrial, biological and pharmaceutical applications [1–9]. The hydroxy anthraquinone chromophore has biological activity in several antitumour anthracyclines [2–4]. Antitumour anthracycline is the most useful group of cytotoxic anticancer drugs, which are commonly used in cancer chemotherapy. They have anthraquinone skeleton and aglycone ring coupled with amino sugar. The disparate substitute in these materials creates unique properties, such as intercalate between DNA, interfering in transcription and replication [5–8].

The molecular activity and medicinal properties of anthracycline derivatives can be determined through stereoisomerism and

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substituting the hydrogen of aglycone ring by groups like alkyls, amines, hydroxyl, etc. The photo-physical behaviors of substituted anthracycline molecules in visible reign are controlled by anthraquinone skeleton. The substituted groups on anthraquinone chromophore can change photo-physical and interactional characters of anthracycline molecules. Along with the substitution effect, media effects can play significant roles in chemical and physical processes of anthraquinone in solutions [10–12]. Therefore, quantitative measurement of the antitumour anthracycline molecules, dipole moment variations and solvent–solute interactions is interesting, due to their therapeutic application [13].

The photo-physical and interactional behaviors of anthracycline arise from either specific (e.g., hydrogen bonding, proton transfer, intramolecular and intermolecular charge transfer (ICT)) or non-specific (dielectric enrichment) interactions with media.

Kamlet, Abboud and Taft's implemented a multi-parameter polarity scale, for quantitative measurement of contribution assessment of different types of media–solute interactions [14–16]. Media or solvent polarity scales [17,18] can evaluate the media effect in quantity. Spectroscopic solvent polarity scales have been derived from solvent-sensitive standard compounds, absorbing or emitting radiation in different spectral ranges, due to variation in their microenvironment polarity [18–23].

Media effect on the spectral features of solute molecule can be interpreted through means of linear solvation energy relationship (LSER), reported by Kamlet–Abboud–Taft equation [14].

$$\upsilon = \upsilon_0 + s \cdot \pi^* + b \cdot \beta + a \cdot \alpha \quad (1)$$

where π^* is a measure of solvent dipolarity/polarizability [24], β is scale of solvent hydrogen bond acceptor (HBA) basicity [25], α is scale of solvent hydrogen bond donor (HBD) acidity [26] and υ_0 is a regression value for the solute property in reference solvent, cyclohexane, or in vacuum. Employing multi-linear regression analysis, the coefficients s, b and a in Eq. (1) can be obtained. These coefficients measure the relative susceptibilities of the solute property (spectral features in this work) to the indicated solvent characteristic.

In this study, spectral features of three anthracyclines were studied in different solvents. The polarities of used solvents cover all application ranges of samples. Obtained results were used to estimate the ground and excited state dipole moments. Moreover, the solvatochromic activities of these anthracycline samples were evaluated quantitatively via multi-parameter solvent polarity scale. Dipole moment variation and solvatochromic behavior of the samples were elucidated as solvent–solute specific and/or non-specific interactions.

Experimental

Materials

The three anthracycline solute samples was purchased from ALEXIS Biochemicals and used without further purification (Table 1). All the solvents used in the study were of highest available purity from Merck, and the spectroscopic solvent polarity parameters of them are given in Table 2.

Absorption and emission spectroscopy

Double beam Shimadzu UV-2450 Scan UV–visible spectrophotometer was used to record the absorption spectra over a wavelength range of 300–800 nm, which is combined with a cell temperature controller. Quartz cuvettes were used for measurements in solution via l × 1 cm. Fluorescence of samples' solutions was studied with a JASCO FP-6200, with standard Quartz cuvettes. The sample concentrations were chosen to be 1×10^{-5} M for all the samples.

Table 1
Molecular structure of anthracycline compounds.

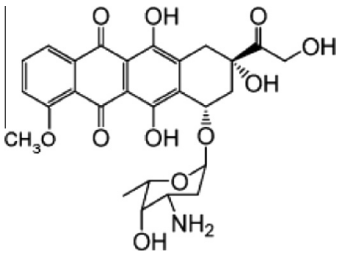
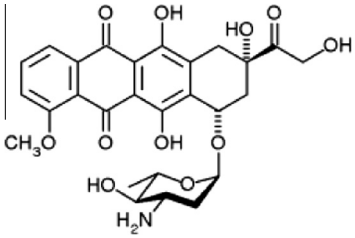
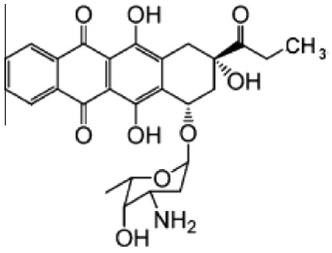
Sample	Molecular weight (g/mol)	Structure
Doxorubicin	580.0	
Epirubicin	580.0	
Idarubicin	533.95	

Table 2
Spectroscopic polarity parameters, physical properties and polarity functions of employed solvents [18].

Solvents	ε	α	β	π^*	$f_{BK}(\varepsilon,n)$	$g_{BK}(n)$	$f(\varepsilon,n)+2g(n)$
1,4-Dioxan	2.22	0.00	0.37	0.49	0.044	0.286	0.617
1-Butanol	17.5	0.84	0.84	0.47	0.750	0.271	1.293
2-Propanol	19.9	0.76	0.84	0.48	0.779	0.256	1.292
Acetone	21.01	0.08	0.48	0.62	0.792	0.244	1.281
Ethanol	24.3	0.86	0.75	0.54	0.812	0.246	1.303
Methanol	33.7	0.98	0.66	0.6	0.857	0.224	1.306
DMF	39.25	0.00	0.69	0.88	0.842	0.292	1.425
DMSO	47.24	0.00	0.76	1.00	0.841	0.324	1.489
Water	78.80	1.17	0.47	1.09	0.914	0.227	1.361

Estimation of the dipole moment

The most common technique for determining dipole moment is based on the solvent spectral shift. In this method, employing the quantum mechanical second order perturbation theory and taking into account the Onsager model of reaction field for a polarizable dipole moment [27–29], leads to expressions for difference and sum of $\tilde{\nu}_a$ and $\tilde{\nu}_f$:

$$\tilde{\nu}_a - \tilde{\nu}_f = m_1 f(\varepsilon, n) + const. \quad (2)$$

$$\tilde{\nu}_a + \tilde{\nu}_f = -m_2[f(\varepsilon, n) + 2g(n)] + const. \quad (3)$$

where

$$m_1 = \frac{2(\mu_e - \mu_g)^2}{hca^3} \quad (4)$$

$$m_2 = \frac{2\left(\mu_e^2 - \mu_g^2\right)}{hca^3} \quad (5)$$