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Research Article

PHARMACEUTICAL ASPECTS OF MICELLAR SOLUBILIZATION OF SALICYLIC ACIDS USING DIFFERENT SURFACTANTS

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ABSTRACT

Fluorescence spectroscopy is a critical tool for exploring interaction between micelles and the molecules. In recent years, extensive researches have been made on the effects of the micelles formed by the different types of surfactants, on diverse systems. Micellar solubilization is widely useful in pharmaceutical industry due to formulation of sparingly soluble drugs in soluble form. This research paper aims to provide unusal approach for the analytical and medical applications of Salicylic acid based on its solubilization in micellar media. Micellar solubilization of Salicylic acids in non-ionic, anionic and cationic surfactants is monitored by fluorescence techniques. Absorption spectra was taken by UV-VIS spectrophotometer. The calculated empirical fluorescence coefficient (k_f) values are in good agreement with the fluorescence intensity. In conclusion the process of solubilization of salicylic acid in micellar medium facilitates the easy drug delivery to the patients.

Keywords: Salicylic acid, Surfactant, Micellar solubilization, Fluorescence spectroscopy.

1. INTRODUCTION

Fluorescence spectroscopy also called as spectrofluorometry is one of the most important experimental tools in several areas of analytical science and pharmacy industry owing to its remarkably high sensitivity and great selectivity. It has several applications across a wide range in biochemistry, biotechnology, environment pollution control and forensic sciences [1]. It requires minor amount of sample because it can detect even a single molecule and enhances spatial and time resolution when combined with microscopic and laser technique respectively [2]. Surfactants have an important characteristic of micelle formation which involves accumulation of colloidal size crystals in solutions. Micelle formation by surfactants is a vital phenomenon from pharmaceutical point of view because of their potential to enhance solubility of substances with sparingly solubility in water [3].

In the recent years Pharma industries and Biotechnology departments are broadly assisted by surfactants since they are employed to a great extent in varied drug dosage to enhance their bioavailability, stability and control wetting along with other properties [4]. "Solubilization is the spontaneous dissolving of substance by reversible interaction with the micelles of a surfactant in a solvent to form a thermodynamically stable isotropic solution with reduced thermodynamic activity of the solubilized material." The solubilization of plasma membrane proteins is essential for the transportation of drugs and other pharmaceutical material across lipid bilayers and membranes [5]. Micellar solubilization is an effective technique used preferably for dissolving hydrophobic compounds in aqueous medium. By Spectroscopy it has been described that different solubilized molecules are dispersed in different areas of micelles [6-7]. Salicylic acid is a phenolic compound which has various medicinal applications. It is used to treat various skin disorders such as warts, calluses, psoriasis, dandruff, acne, ringworm and ichthyoids [8]. The present research aims to investigate the pharmaceutical potential of micellar solubilization of salicylic acids in anionic, cationic and non-ionic surfactants in the interest of catalyzing drug delivery system.

2. MATERIAL AND METHODS

2.1. Experimental

All the fluorimetric analyses were carried with a synchronized strip chart recorder (Model No. 056) with Perkin Elmer Fluorescence Spectrophotometer (Model

No. 204 A). A Xenon lamp acted as a lighting source. The absorption spectra were taken by UV-VIS Spectrophotometer. The experiments were carried out at room temperature. The stock solution of salicylic acid was made in double distilled water. For fluorescence studies the compound concentration was held at $7x10^{-6}$ M and for absorption studies at 1 x 10^{-4} M. The concentration of the compound was kept constant throughout the experiment. The surfactants employed for solubilization of salicylic acid are shown in Table-1.

Table1: Surfactants employed for solubilization of salicylic acid

S. No.	Surfactants category	Name of the Surfactants
1.	Non-ionic surfactants	i) Polyoxyethylene Tert–octyl Phenol (Triton X – 100) ii) Polyoxyethylene Sorbitain Monolaurate (Tween – 20) iii) Polyoxyethylene Sorbitain Monooleate (Tween – 80)
2.	Anionic surfactants	i) Dodecylbenzene Sodium Sulphonate (DBSS) ii) Dioctyl Sodium Sulphosuccinate (DSSS) iii) Sodium Lauryl Sulphate (SLS)
3.	Cationic surfactants	i) Cetylpyridinium Chloride (CPC) ii) Cetyltrimethyl Ammonium Bromide (CTAB) iii) Myristyltrimethyl Ammonium Bromide (MTAB)

All the surfactants were either of BDH (UK) or Sigma (USA) products. Using surface tension calculation, the purity of the surfactants was tested by determining their CMC value using drop weight method. The values obtained coincide with reported values. The absolute fluorescence quantum yield values of salicylic acid calculated relative to anthracene are in the same range as that of salicylic acid. Approximate corrections were made to compensate for different absorption of the compound and standard.

2.2. General Procedure

Each time the total fluorescence emission intensity was calculated for the normal and the fluorescence region over the entire range of emission spectra under equivalent conditions. Molar extinction coefficient data was shown as its logarithm (log Ɛ). The Stokes' shift results were also correlated with change in its concentration.

3. RESULTS AND DISCUSSION

The aqueous solution of salicylic acid demonstrated maximum excitation peak at 295 nm and emission peak at 410 nm. On addition of nonionic surfactants, TX-100 and Tween-80, the fluorescence intensity decreased continuously, while Tween-20 caused small enhancement in fluorescence intensity at its higher concentration. The fluorescence spectrum changes of salicylic acid when Tween-20 is added are given in Fig. 1. In addition to salicylic acid solution, all the anionic surfactants induced a continuous increase in the intensity of its fluorescence emissions with increasing concentration. DBSS has exerted the greatest impact among these with blue shift of 55 nm. The changes in salicylic acid fluorescence intensity on adding DBSS are shown in Fig. 2. CTAB and MTAB added solution fluorescence intensity for cationic surfactants initially marginally decreased and then increased at their higher concentration with a blue shift of 5 nm in emission peak position while CPC had a significant decreasing effect on the salicylic acid fluorescence intensity. The maximum effects of CTAB on salicylic acid are given in Fig. 3. Fluorescence intensity in the presence and lack of surfactants is shown in the Table 2.

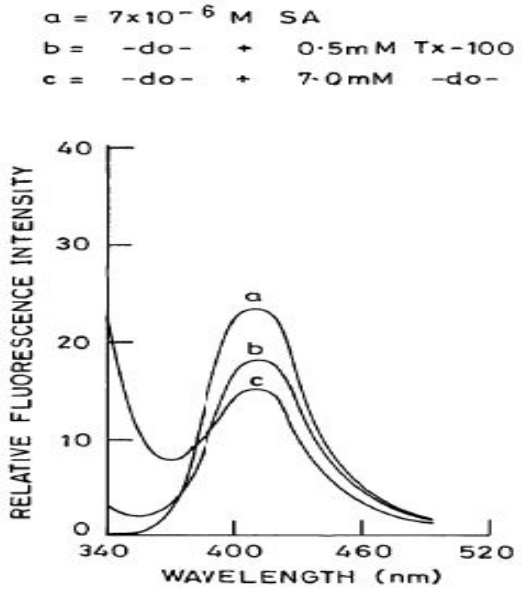

Fig. 1: Fluorescence spectrum changes of salicylic acid when Tween-20 is added

The absorption spectra of salicylic acid produced a peak at 295 nm. All non-ionic surfactants showed an increase in absorption. TX-100 and Tween-80 showed a blue shift of 20 nm in peak position, while Tween-20 did not show any shift in λ_{max}. All the three anionic surfactants showed an increase in absorbance without any shift in λ_{max}. For all cationic surfactants absorbance initially decreased and then increased with a red shift of 5 nm. The changes in the SLS absorption spectra are shown in Fig. 4.

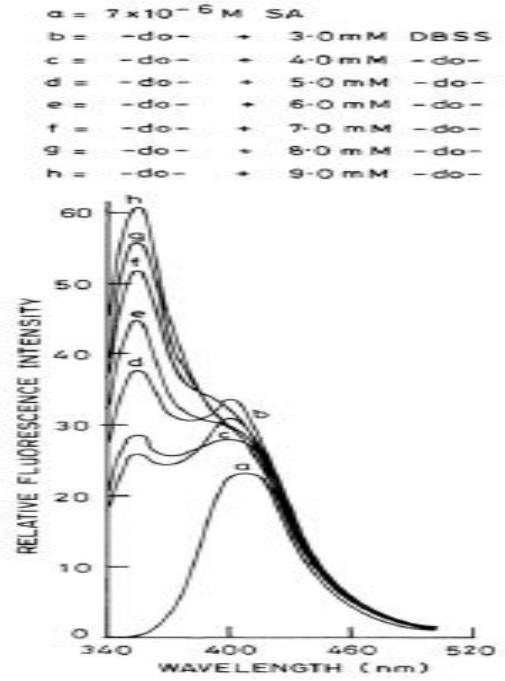

Fig.2: Changes in salicylic acid fluorescence intensity on adding DBSS

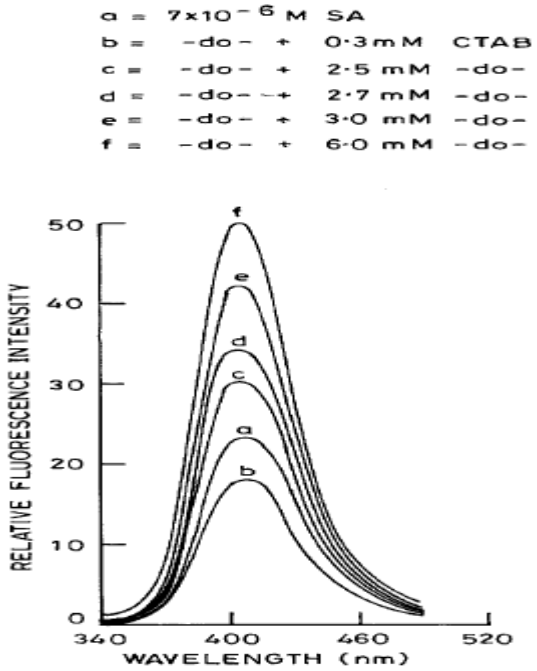

Fig.3: Maximum effects of CTAB on salicylic acid

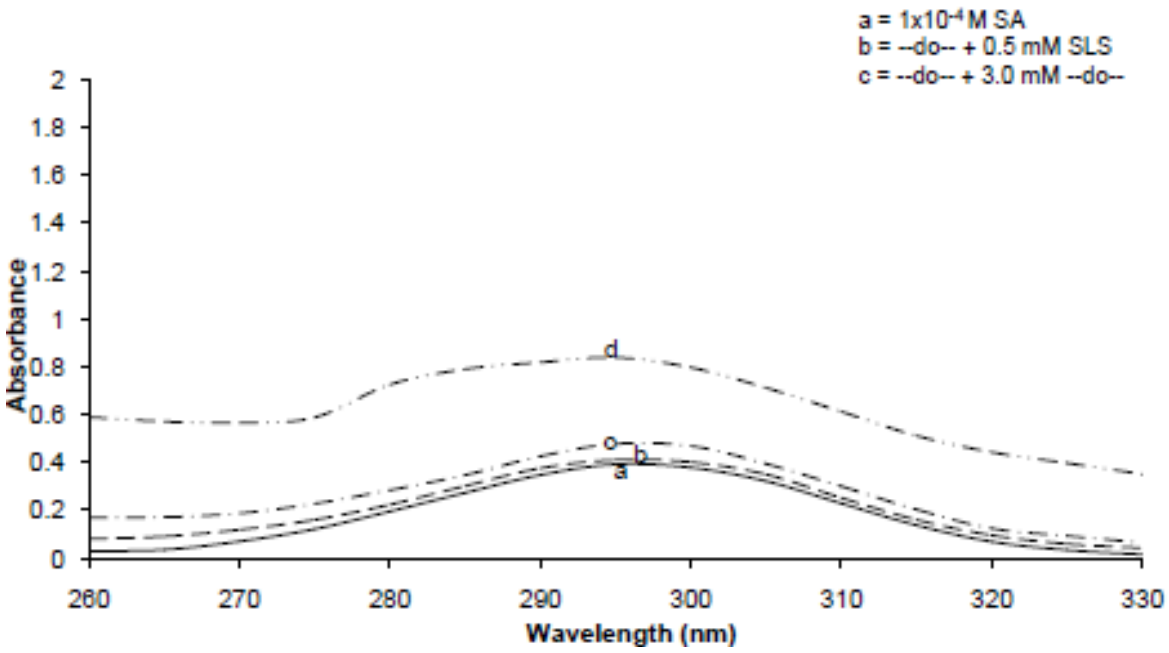

Fig.4: Changes in the SLS absorption spectra

Table 2: Fluorescence intensity of Salicylic acid in absence and presence of surfactants

λ_{ex}= 295 nm; λ_{em}= 410 nm; P.M. Gain= 3; Sensitivity Range= 0.3

Name of Surfactant	Fluorescence intensity in absence of surfactant	CMC's of surfactant (mM)	Concentration of surfactant used (mM)	Relative fluorescence intensity	λ_{em} (nm)
TX-100	23	0.26	8.0	15	410
Tween-20	23	0.05	8.0	32	410
Tween-80	23	0.1	8.0	16	410
DBSS	23	0.81	9.0	61	355
DSSS	23	0.91	9.0	30	410
SLS	23	8.2	9.0	33	410
CPC	23	0.6	5.0	0	410
CTAB	23	0.90	7.0	51	405
MTAB	23	3.6	7.0	47	405

The calculated fluorescence quantum yield (ϕ_f) and empirical fluorescence coefficient (k_f) values of surfactant added salicylic acid appeared almost parallel with fluorescent intensity shifts in the compound. For nonionic surfactants, the TX-100 and Tween-80 quantum yield (ϕ_f) values decreased by increasing their concentration, while with the Tween-20 quantum yield values increased. With all anionic surfactants ϕ_f values continuously increased. Highest ϕ_f values are obtained for DBSS micellar media, which are given in Table-3. For cationic surfactant CPC, ϕ_f values decreased. The ϕ_f values decreased initially and then rise with CTAB and MTAB. For both nonionic and anionic surfactants, the molar extinction coefficient (log ε) values increased. While with cationic surfactants log ε values gave different trend. With all the three cationic surfactants log ε values initially decreased and then increased at their higher concentrations. The Stokes' shift values at room temperature increased on dilution of salicylic acid solution. The calculated Stokes' shift values are given in Table- 4. On the basis of solubilization by micro heterogeneous environment of micelles present in the surfactant solution at or slightly above CMC, the results obtained can be clarified. Improved fluorescence strength of the compound by adding surfactant can be due to rising fluorescence quantum efficiency.

Table 3: Absorption maxima (λ_{max}), fluorescence maxima (λ_{em}), molar extinction coefficient (log ε) and quantum yield (ϕ_f) of salicylic acid at different concentration of DBSS (mM)

S. No.	Concentration of DBSS (mM)	λ_{max} (nm)	log ε ($dm^3mol^{-1}cm^{-1}$)	λ_{em} (nm)	ϕ_f
1.	0.00	295	4.7481	410	0.2395
2.	3.0	295	4.8521	405	0.3352
3.	5.0	295	4.8692	400	0.4028
4.	9.0	295	4.9286	355	0.4391

As the surfactants are applied to the aqueous solution of compounds, the surfactant micelles get adsorbed at the interfaces and eliminate the hydrophobic groups from water interaction, thus reducing the system's free energy and favoring micellization. However, in moving the hydrophobic groups from solution to micelle in the solvent, there may be some loss of freedom restricted to the micelle and, in reference to the ionic surfactants, electrostatic repulsion from other similarly charged surfactant molecules in the micelle. Such forces increase the system's free energy, and thus resist micellization. Therefore, whether micellization occurs in specific instance and in that case at what concentration of monomeric surfactant, depends on the balance between the factors which promote and oppose micellization. The increase in quantum yield therefore implies that the surfactants DBSS, DSSS, SLS, CTAB and MTAB have solubilized the suspended solubilizate molecules (Salicylic acid), which are dispersed as macro crystals in water which colloid with anionic micelles to penetrate into the micellar core interior. Here the anionic micelles have formed 1:1 complex with the protonated solubilized molecules. This complex is called ion association complex [9].

Table 4: Stokes' shift data of Salicylic acid at room temperature

S. No.	Concentration of Compound	λ_{ex} (nm)	F.I.	λ_{em} (nm)	F.I.	P.M. Gain	Sensitivity Range	Stokes' Shift (cm^{-1})
1.	$1x10^{-3}$ M	315 280	36 19	410 410	52	3	0.1	7355 11324
2.	$7x10^{-4}$ M	310	43	410	63	3	0.1	7867
3.	$5x10^{-4}$ M	305	55	410	83	3	0.1	8396
4.	$3x10^{-4}$ M	300	60	410	89	3	0.1	8943
5.	$1x10^{-4}$ M	295	42	410	63	3	0.1	9508
6.	$7x10^{-5}$ M	295	34	410	50	3	0.1	9508
7.	$5x10^{-5}$ M	295	81	410	OR	3	0.3	9508
8.	$3x10^{-5}$ M	295	53	410	79	3	0.3	9508
9.	$1x10^{-5}$ M	295	19	410	28	3	0.3	9508
10.	$7x10^{-6}$ M	295	16	410	23	3	0.3	9508
11.	$5x10^{-6}$ M	295	10	410	15	3	0.3	9508
12.	$3x10^{-6}$ M	295	7	410	10	3	0.3	9508
13.	$1x10^{-6}$ M	295	3	410	6	3	0.3	9508

OR= Out of Range

Owing to intramolecular hydrogen bond formation in both, TX-100 and Tween-80, they have quenched the fluorescence intensity. Thus there is no effective hydrogen bond between the solubilizate and surfactant micelles. The quenching also revealed that, especially for TX-100, the compound prefers the hydrophobic core to the hydrophilic poly (ethylene oxide), a PEO shell. Clearly, compound fluorescence in the core is greatly reduced as in non-aqueous solvents. This means that the compound is not hydrated around the aromatic rings found within the core [10]. Quenching can also be induced by non-radiative energy loss from the excited molecules. Absorption spectrum of the compound is not affected by the addition of TX-100 or Tween-80 in the concentration range used in fluorescence quenching experiment. This reveals that there is no complex formation or association of the solubilizate with the quencher in the ground state and the quenching occurs only due to interaction of excited solubilizate molecule and quencher. Hence it is not static but dynamic in nature. The addition of CPC was also detected to quench fluorescence, which may be due to the preferential electrostatic interaction between the polar substituents of salicylic acid molecules and the surfactant's cationic head component, resulting in a shift in the configuration of the solubilized molecule in which it loses coplanarity. The fluorescence decline can also be due to the interaction between the л-electron system of the excited fluorophore state and the quencher molecule (CPC) attributed to the prevalence of nucleophilic pyridine ring in the structures, which allows it act as a quencher through the hydrogen bond between the proton donor and the acceptor. This would contribute to the delocalisation of the excited state's electrons and ultimately to the fluorescence declination [11]. Absorption is less environmentally sensitive than fluorescence, so the absorption spectra might be less influenced by the addition of surfactants particularly in comparison to the fluorescence spectrum. A progressive improvement in absorbance occurred on addition of all three types of surfactants. The blue shift in absorption maxima may be because of gap between the solvation energies of the solute in ground and excited state.

The significant value of log ε is allocated to the π-π^* transitions. The high quantum yield (ϕ_f) values in micellar medium mainly owing to the rates of non-radiative processes which are lower in micellar medium compared to those in aqueous medium [12]. It might be resulting from fluorophore absorption on the micellar surface, which reduces the chances of collosional fluorophore deactivation by water molecules [13]. The large magnitude of Stokes' shift of Salicylic acid is owing to formation of hydrogen bond between the solute and the solvent in ground state, resulting into the breaking of this bond following excitation to S_1 but reforms proton transfer [14]. The excited hydrogen bonded state can be generated via two routes as shown in the following scheme where S represents the solvent molecule and A is the fluorophore [15].

$$A + S \rightarrow AS \xrightarrow{h\nu} [AS]^*$$

$$A^* + S \rightarrow [AS]^*$$

The calculated empirical fluorescence coefficient (k_f) values are in good agreement with the fluorescence intensity. The obtained values of K_f can be due to the enhanced sensitivity of the fluorescence analysis of the solubilization of organic molecules by surfactants providing a safe microenvironment, resulting in an improved solubilization of fluorescence by shielding the excited state from non-radiative decay often encountering in bulk aqueous solution.

4. CONCLUSION

After analyzing and comparing these results obtained for salicylic acid, it is established that all the theoretically determined spectral parameters are in close agreement with the experimental outcomes. This proves the validity of the assumption made. Thus, it can be generalized from the present fundamental study to the understanding of assimilation of some essentially important drugs in the human body by phospholipids, which acts as micellar in body fluid. The process of micellization followed by solubilisation of Salicylic acid substrate would catalyze drug delivery activities. Micellar solubilisation of Salicylic acid finds an extensive application in biochemical and biomedical fields.

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Declaration of conflicting interests

The Authors declare no conflict of interest while preparing this research paper.

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