



Comparison Between Interaction of Hydrophobic-anionic and Hydrophobic-cationic Mixed Micellar System with Drug Ciprofloxacin

V. C. EZHILRANI¹, VIGNESHWARI. R² and SASMITA DASH^{3*}

^{1,2,3}Department of Chemistry, Annamalai University, Chidambaram-608002, Tamil Nadu, India.

*Corresponding author E-Mail: mishra342sas@gmail.com

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ABSTRACT

The interaction studies of drug ciprofloxacin with two mixed micellar systems are reported. The mixed micelles comprise a nonionic hydrophobic surfactant, pluronic L-81, an anionic surfactant, Ammonium dodecyl sulfate (ADS); and a cationic surfactant, Cetylpyridinium bromide (CPB). The various combinations chosen were L-81-ADS and L-81-CPB. The properties of both the mixed micelles were compared. Spectrophotometric, conductometric, co-solvent effect, and Infrared studies were used for the investigations. The studies were carried out in a wide range of mixed micellar concentrations in the post micellar region of the individual surfactants. The solubilization of drug CPX in the L-81-ADS was higher than that in L-81-CPB mixed micelle, as evidenced by UV studies. Ethanol and ethylene glycol were found to be effective co-solvents for both the mixed micellar systems. The conductivity studies of CPX with ADS and CPB surfactants, displayed a higher value of conductance for CPX and ADS, from $0.37\mu\text{s}^{-1}$ to $0.74\mu\text{s}^{-1}$ compared to CPX and CPB. The drug-mixed micelle displayed a higher molecular weight complex formation as seen from the IR spectra.

Keywords: Surfactant, Solubilization, UV-visible spectrum, Co-solvent effect, Conductometric studies.

INTRODUCTION

In the nonionic group of surfactants, the triblock copolymer class has received a lot of attention. The commercial trade name is pluronic or poloxamer. These amphiphilic polymers have polypropylene oxide (PPO) and polyethylene oxide (PEO) in a single entity¹. They are commercially available in a wide range of molecular weights and PEO/PPO ratios and hydrophilicity/hydrophobicity². The pluronic with varying PO/EO ratio and the

molecular weights displays a number of interesting properties. Also, they display various morphologies such as spherical, cylindrical micelles, vesicles, and various crystalline phases³. When the copolymers are dissolved in water they exist as unimers at low temperature and concentration. Above the CMC or critical micellization temperature (CMT), however, they self-aggregate to core-shell micelles like other surfactants⁴.

Pluronic have widespread applications in



emulsification, solubilization, detergency, foaming, lubrication, cosmetics formulation, and inks⁵. They also have specialized applications in the pharmaceutical industry. They help in the controlled release of drugs from micelles⁶. Micelles form a hydrophobic core mainly consisting of weakly hydrated PO which encapsulates blocks surrounded by an outer shell of fully hydrated EO blocks⁷. Several reports have proved that the cleansing property and irritation potential of surfactants can be controlled with the addition of pluronic⁸. Copolymers have been proved to be effective in intracellular delivery due to the presence of the oxyethylene group in corona⁹. Triblock copolymers interact with ionic surfactants. They are widely used in the solubilization of drugs¹⁰. In the category of pluronic, F127 has wide application in drug delivery to tissues. The EO/PO ratio, molecular weight, and the hydrophilic-lipophilic balance (HLB) of block copolymer control the self-associative behavior of the pluronic surfactants¹¹.

Cetylpyridinium bromide (CPB) is a cationic surfactant with a molecular formula $C_{21}H_{38}BrN$ (molecular weight 384.4g/mol). Cationic surfactants based on quaternary ammonium salts are found in various industrial and commercial products¹². Quaternary pyridinium is one of the common cationic surfactants¹³. They are widely used in emulsion, polymerization, corrosion, inhibitors, antimicrobial agents, and some drugs due to their stability as emulsions and their bacteriostatic properties¹⁴.

Because of the antibacterial property, they are used as disinfectants and also in the treatment of mouth, throat, skin, and eye infections. CPB is used in fabric processing and extraction of metal. CPB has a cationic quaternary pyridinium head and a C16 hydrophobic tail¹⁵. It has similar usage as cationic pyridinium surfactants in industry, household applications, and pharmaceuticals. A variety of procedures, such as an ion-selective electrode, high-performance liquid chromatography, flow injection analysis, capillary electrophoresis, gas chromatography, mass spectrometry techniques are used to determine quaternary ammonium salts in cationic surfactants¹³.

Ammonium dodecyl sulfate (ADS), an anionic surfactant has a molecular formula $(CH_3(CH_2)_{10}CH_2OSO_3NH_4)$, molecular weight 283.

43 g/mole). ADS is a strong solubilization reagent that is commonly used for extracting protein. It is primarily used in shampoos and body wash as a foaming agent¹⁶ lauryl sulfates are very high foam surfactants that reduce the surface tension of water by forming micelles at the air-liquid interface¹⁷.

ADS is less hydrolyzed in acidic solutions and displays less skin irritation compared to SDS. For these reasons, there is more use of ADS in the cosmetic and toiletry industry¹⁸. Shampoos contain up to 31% ADS. Above the CMC, the anions organize into a micelle, in the form of a sphere with the polar, hydrophilic head of ADS.

Ciprofloxacin is a broad-spectrum drug used for the treatment of bacterial infections. It belongs to the fluoroquinolone class. The enhanced spectral activity of the drug is due to the position of the fluorine atom at the sixth position and the piperazine ring at the seventh position. The solubility of CPX showed increased solubility in the presence of metal cations. They are useful for the treatment of serious infections, especially against gram-negative bacteria¹⁹. The antibacterial efficiency of the drug CPX is due to two enzymes involved in bacterial DNA synthesis, which leads to bacterial cell death. CPX is widely used to cure joint infections, intra abdominal infections, respiratory infections, skin infections, typhoid fever, and urinary tract infections, etc. CPX has low solubility which leads to the potential decrease of bioavailability. Compared to single pluronic, mixed micelles display improved properties such as stronger binding capacity, enhanced drug loading efficiency, and better biocompatibility. Hence, mixed micelles are used for microbial therapy to deliver the drug to the infection site²⁰.

Interaction of Ciprofloxacin drug in pluronic micelle and mixed micellar medium (nonionic-nonionic combination) has already been studied²¹. It was of interest to observe the interaction of Ciprofloxacin with mixed micelle having a negatively charged surfactant like nonionic-anionic (L-81-ADS) and nonionic-cationic (L-81-CPB) with a pluronic surfactant.

EXPERIMENTAL

Materials

Ciprofloxacin was obtained as a gift sample from MMC health care, Ltd. Chennai, and was used

for characterization, pluronic L-81, Cetylpyridinium bromide (CPB) 90%, Ammonium lauryl sulfate (ADS), ethanol (99% purities) and ethylene glycol (99%) were obtained from Sigma Aldrich Chemicals Ltd. Double distilled water was used for all the experiments.

Preparation of mixed micellar system

A stock solution of pluronic L-81 (5%wt) was prepared in double-distilled water and kept in cold condition at 5°C. The molecular weight of cationic surfactant Cetylpyridinium bromide (CPB) was 384.4g/mol and stock solution 50mM of CPB was prepared. A stock solution of 60mM of anionic surfactant, Ammonium dodecyl sulfate (ADS) (molecular weight, 283.43g/mol) was prepared. Ethanol and Ethylene glycol were directly used for the experiment without further purification. The number of individual surfactants used for mixed micelle was different for different experiments. The quantities, therefore, are mentioned in the individual tables. However, care was taken to use all the concentrations of individual surfactants well above CMC to ensure complete micellization.

Preparation of the drug sample

Aqueous solution of drug ciprofloxacin was prepared by taking 0.05 g of the drug dissolved in 100 mL double distilled water. Different concentrations of cationic, anionic surfactants were added to pluronic L-81 to prepare drug encapsulated mixed micellar systems.

UV-spectroscopic measurement

A Shimadzu (UB-1650) PC spectrophotometer was used for determining the solubility of the drug. The solubilized drug was measured at λ_{max} of 271nm. CPX stock solution was prepared (0.05 g CPX in 100 mL water). From the stock solution of 5% pluronic L-81, 50mM of CPB, and 60mM ADS, various combinations were prepared as mentioned in the individual tables and spectrophotometric measurements were carried out.

UV-spectroscopic measurement in addition of co-solvent effect

Surfactants are referred to as amphiphilic molecules. Because the polar group has a large

affinity for polar solvents. In this experiment we have used two different co-solvents, viz., ethanol and ethylene glycol. The solutions were prepared by using different concentrations of surfactants to which a fixed volume of solvents was added and the changes were noted from UV measurement.

FTIR measurement

From the stock solutions, 2% neat and mixed micelle solutions were prepared. The FTIR studies were done by using Cary-630. FTIR agilent technology in the range of 400-4000 cm^{-1} . The volume of two ml each of pluronic L-81, CPX, ADS, and CPB were taken. The concentration of the drug was kept constant in all the samples. The spectrum for OH stretching vibration arising due to water was common for all the five aliquots because of the aqueous medium, hence ignored.

Conductivity measurement

Conductance measurements were made by using a specific conductivity meter PICCO-180 and platinum electrode dipped in the solution. The specific conductance measurements were carried out for the platinum electrode at 300K. Experiments were carried out by adding different concentrations of the stock surfactant solutions and conductivity was measured with and without drug CPX. All the concentrations chosen were well above the CMC of the individual surfactants.

RESULT AND DISCUSSION

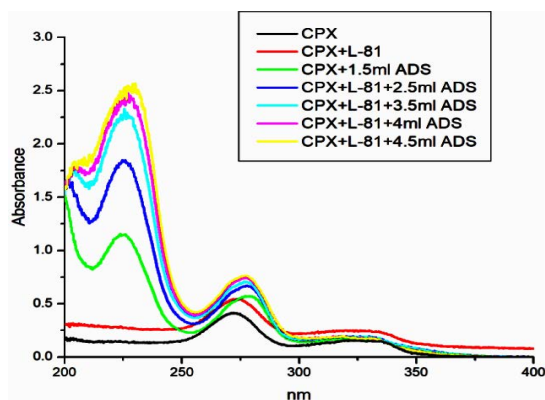
UV-visible spectra

UV-visible spectra of drug CPX alone, and CPX in presence of a nonionic hydrophobic surfactant, pluronic L-81, cationic surfactant CPB, and anionic surfactant ADS and their mixed micelles were recorded. The results are displayed in Table 1, Table 2, Fig. 1, and Fig. 2. The spectra of drug CPX only was carried out in the first step. The absorbance at 271 nm was noted. In the next step spectra for drug CPX with pluronic L-81, CPX with ADS and CPX with CPB were recorded. The starting concentration of L-81 and ADS used in the experiment was 0.09 mM and 9 mM respectively. They were well above the CMC of the respective surfactants.

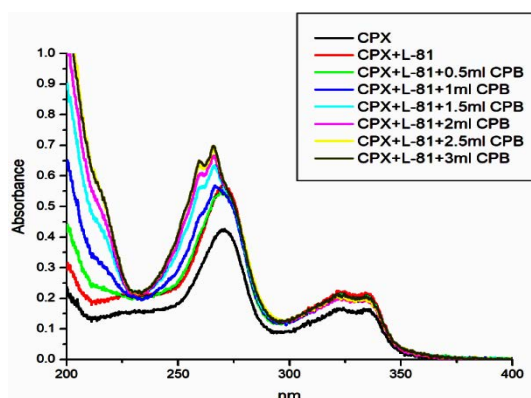
Table 1: UV-absorption spectra of drug CPX and CPX in presence of L-81, ADS and mixed micelle of L-81-ADS

Sl. No	CPX mL	L-81 mL	ADS mL	Water mL	λ_{\max} nm	Absorbance
1	1	0	0	9	271	0.417
2	1	1	0	8	271	0.548
3	1	0	1.5	7.5	271	0.574
4	1	1	2.5	5.5	271	0.674
5	1	1	3.5	4.5	271	0.709
6	1	1	4	4	271	0.748
7	1	1	4.5	3.5	271	0.765

From Table 1 and Fig. 1 it can be observed that the absorbance of only drug CPX at λ_{\max} 271nm was 0.417. In addition to pluronic L-81, there was an increase in absorbance to 0.548. Even though L-81 is a hydrophobic surfactant with a low HLB (HLB=2), still for the drug CPX there is more encapsulation of the drug in the single micellar medium of L-81. The addition of ADS to the drug CPX enhanced the absorbance to 0.574 which is not only higher than CPX absorbance, also higher than L-81 and CPX. This indicates that there is a higher affinity of the drug CPX to be encapsulated in the anionic micellar medium.

**Fig. 1. Absorbance of Ciprofloxacin with ADS, L-81, and ADS+L-81 mixed micellar system**

In the next step, the fourth aliquot was taken as a combination of L-81 and ADS with CPX, and the spectra were recorded. This time the absorbance was higher (0.674) for CPX-mixed micellar combination compared to the two CPX-single micelle combinations i.e. CPX-L-81 and CPX-ADS. Hence, it can be concluded that for the drug CPX the particular mixed micellar system is effective for enhanced solubilization of the drug in the micellar core.

**Fig. 2. Absorbance of Ciprofloxacin with CPB, L-81, and CPB+L-81 mixed micellar system**

Keeping the nonionic L-81 concentration constant, a varying range of anionic ADS was added and its effect (solubilization) of the drug was observed at λ_{\max} . There was a progressive increase in the drug solubilization on the increased concentration of ADS as observed from the absorbance. This further indicates that a higher concentration of the anionic surfactant ADS in the mixed micellar combination can enhance the drug encapsulation in the mixed micelle.

The spectra of neat CPX drug showed an absorbance 0.430 at λ_{\max} 271nm. From Table 2 and Fig. 2 it can be observed that the addition of pluronic L-81 increased the absorbance to 0.571. But, the addition of the cationic surfactant CPB decreased the absorbance compared to L-81, but it was more than the absorbance of CPX alone. With the L-81 and CPB mixed micelle, however, the drug CPX displayed an intermediate absorbance value compared to L-81-CPX and CPB-CPX combinations. This points to the fact that the mixed micellar system did not have any additional encapsulation efficiency compared to a single micellar system with CPX. The probable reason for this may be a cationic head group of the surfactant (pyridinium bromide) is not readily accommodating as many CPX molecules in the micellar core as it did in a L-81-anionic combination. Also, there was probable repulsion of the cationic-cationic head groups in mixed micelle because of high molecular weight. Interestingly in this mixed micellar system, there is an isosbestic point at 277nm, which means about 6nm red-shifted from the normal λ_{\max} of CPX. The redshift may be due to (i) the formation of a bigger particle size arising from the complex formation with CPB. (ii) This may also be caused by the interaction

between the dipoles of the two monomer units in a head-to-tail manner.

Table 2: UV-absorption spectra of drug CPX and CPX in presence of L-81, CPB and mixed micelle of L-81-CPB

Sl. No	CPX mL	L81 mL	CPB mL	Water mL	λ_{max} nm	Absorbance
1	1	0	0	9	270	0.43
2	1	1	0	8	270	0.571
3	1	1	0.5	7.5	270	0.538
4	1	1	1	7	270	0.548
5	1	1	1.5	6.5	270	0.57
6	1	1	2	6	270	0.58
7	1	1	2.5	5.5	270	0.586
8	1	1	3	5	270	0.591

But, as the concentration of the CPB was increased in the mixed micellar formation keeping the L-81 concentration constant, there was a gradual increase in the absorbance value. This suggests that a higher concentration of CPB is required for the mixed micellar combination for achieving better encapsulation efficiency of CPX in the mixed micellar.

Effect of co-solvents

Co-solvents are used to enhance the solubility of hydrophobic solutes²²⁻²⁷. When they are used along with surfactants their performance further increases in an aqueous medium. Generally, the co-solvents used are water-miscible alcohols. In this study, we have tried to observe the effect of two co-solvents namely ethanol and ethylene glycol on the mixed micellar system.

The drug CPX solubilization was first tried in the above mixed micellar mediums. To improve this further in an aqueous solution, attempts were made to use the co-solvents in the above system.

Ethanol as co-solvent effect

UV-visible study of the above mixed micellar system in presence of ethanol was carried out. There were different observations for anionic and cationic surfactants. In presence of the anionic surfactant ADS, the CPX encapsulated mixed micellar system displayed higher absorbance value. In addition, there was a blue shift by 3 nm (at 268 nm). As seen from Table 3 and Fig. 3, there was also an isosbestic point which indicated that there is a compound formation arising from the combination of pluronic L-81, ADS, CPX, and ethanol Table 3, Fig. 3. This compound formation displayed higher absorbance

values in a progressive manner with increasing ADS concentration. This may be noted here that the other three concentrations i.e., L-81, CPX, and ethanol were kept constant for all the aliquots Table 3. The increase in absorbance suggests that there is more number of CPX molecules entrapped in the mixed micellar system. It was further observed that with the same concentration of L-81, CPX, and ADS the absorbance value was higher in presence of ethanol (aliquots no. 6, Table 3, 0.74) compared to that without ethanol (aliquot no. 4, Table 1, 0.674). The following justifications can be given.

Table 3: UV-absorption spectra of drug CPX and CPX in presence of L-81, ADS and mixed micelle of L-81-ADS, and ethanol as co-solvent

Sl. No	CPX mL	L81 mL	ADS mL	Ethanol (C ₂ H ₅ OH) mL	Water mL	λ_{max} nm	Absorbance
1	1	0	0	0	9	278	0.402
2	1	0	0	2	7	278	0.515
3	1	1	0	2	6	278	0.605
4	1	0	1.5	2	5.5	278	0.66
5	1	1	1.5	2	4.5	278	0.646
6	1	1	2.5	2	3.5	278	0.74
7	1	1	3	2	3	278	0.761
8	1	1	4	2	2	278	0.827

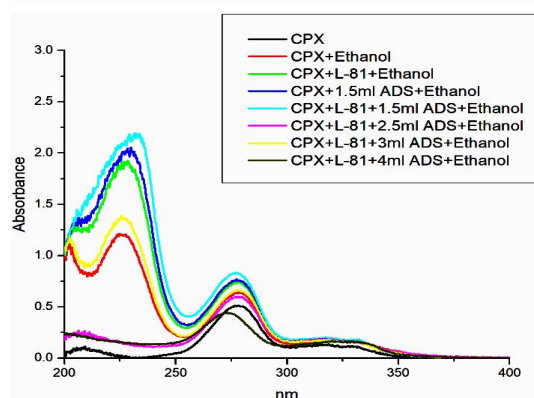


Fig. 3. Absorbance CPX, CPX+ L-81+ADS with ethanol as co-solvent

There exists a polymer co-solvent Vanderwaal's attraction interaction between L-81-ethanol. There also exists a mechanism of this interaction in presence of drug CPX and anionic surfactant ADS. The mechanism here drives the polymer to swell to accommodate more CPX molecules in the mixed micellar system. Hence, it is probable that there is a lowering of the free energy of the system due to the microscopic interactions. As a result, there is an increase in solubility of drug CPX in the mixed micellar system in presence of the co-solvent ethanol.

The cationic surfactant CPB however showed slightly different behavior. There was a redshift by 7nm (at 278nm) for all the aliquots. There was no new peak formed, neither there was any isosbestic point. There was an increase in absorbance with an increase in CPB concentration keeping the concentration of L-81, CPX, and ethanol constant. This pointed at the fact that there were more drug CPX molecules accommodated in the micelle in presence of ethanol. This can be observed by comparing the aliquot 5 of Table 2 (absorbance=0.570) with aliquot 7 of Table 4 (absorbance=0.684). In this case also there lays the Vanderwaal's interactive force operating between the polymer and co-solvent in presence of the drug which facilitates the drug capturing capacity of the mixed micelle.

Table 4: UV-absorption spectra of drug CPX and CPX in presence of L-81, CPB and mixed micelle of L-81-CPB, and ethanol as co-solvent

Sl. No	CPX mL	L81 mL	CPB mL	Ethanol (C ₂ H ₅ OH) mL	Water mL	λ_{max} nm	Absorbance
1	1	0	0	0	9	278	0.491
2	1	0	0	2	7	278	0.539
3	1	1	0	2	6	278	0.541
4	1	0	0.5	2	6.5	278	0.592
5	1	1	0.5	2	5.5	278	0.674
6	1	1	1	2	5	278	0.602
7	1	1	1.5	2	4.5	278	0.684
8	1	1	2	2	4	278	0.626
9	1	1	2.5	2	3.5	278	0.806
10	1	1	3	2	3	278	0.701

Ethylene glycol as co-solvent effect

The mixed micellar system of pluronic L-81 and ADS with drug CPX was subjected to ethylene glycol as a co-solvent medium. Here the anionic and cationic surfactants had almost similar types of interactions as observed from their UV-spectra, no extra peak formed in both cases. There was a redshift by 6nm (λ_{max} =277 nm) for both anionic and cationic surfactants.

As is seen from Table 5 and Fig. 4, there was a progressive increase in the absorbance value with an increase in the concentration of anionic surfactant ADS while the other three concentrations i.e. pluronic L-81, CPX, and ethylene glycol were kept constant. This indicates that at a higher concentration of ADS there are more CPX molecules

entrapped in the mixed micelle. The polymer and co-solvent interaction in presence of CPX and ADS may be of Vanderwaal's attraction leading to the increase in the size of the mixed micellar size which can entrap more CPX molecules. Comparison of aliquot 4 of Table 1 (absorbance=0.674) with aliquot 6 of Table 5 (absorbance=0.749) indicates that there is a clear indication of more solubility of CPX in presence of ethylene glycol compared to without it.

Table 5:UV-absorption spectra of drug CPX and CPX in presence of L-81, ADS and mixed micelle of L-81-ADS, and ethylene glycol as co-solvent

Sl. No	CPX mL	L81 mL	ADS mL	Ethylene GYLCOL mL	Water mL	λ_{max} nm	Absorbance
1	1	0	0	0	9	277	0.535
2	1	0	0	2	7	277	0.578
3	1	1	0	2	6	277	0.6
4	1	0	1.5	2	5.5	277	0.806
5	1	1	1.5	2	4.5	277	0.675
6	1	1	2.5	2	3.5	277	0.749
7	1	1	3	2	3	277	0.884
8	1	1	4	2	2	277	0.945

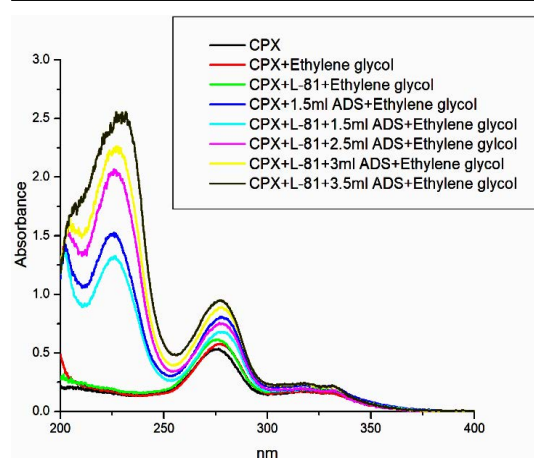
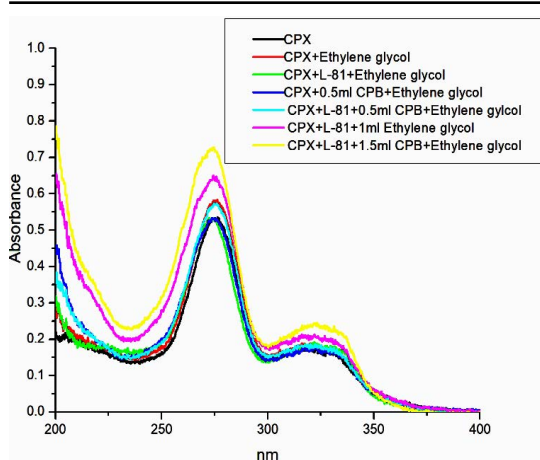


Fig. 4. Absorbance CPX, CPX+ L-81+ADS with ethylene glycol as co-solvent

In the case of cationic surfactant CPB, a similar effect was observed Table 6, Fig. 5. There was an increase in absorbance with an increase in the concentration of CPB keeping L-81, CPX, and ethylene glycol concentration constant. Comparison of aliquot 3 of Table2(absorbance=0.538) with aliquot 5 of Table 6 (absorbance=0.562) suggests that the co-solvent effect was clearly visible with higher solubilization of drug CPX in the mixed micellar system.

Table 6: UV-absorption spectra of drug CPX and CPX in presence of L-81, CPB and mixed micelle of L-81-CPB, and ethylene glycol as co-solvent

Sl. No	CPX mL	L81 mL	CPB mL	Ethylene GYLCOL mL	Water mL	λ_{max} nm	Absorbance
1	1	0	0	0	9	277	0.535
2	1	0	0	2	7	277	0.574
3	1	1	0	2	6	277	0.505
4	1	0	0.5	2	6.5	277	0.52
5	1	1	0.5	2	5.5	277	0.562
6	1	1	1	2	5	277	0.627
7	1	1	1.5	2	4.5	277	0.704

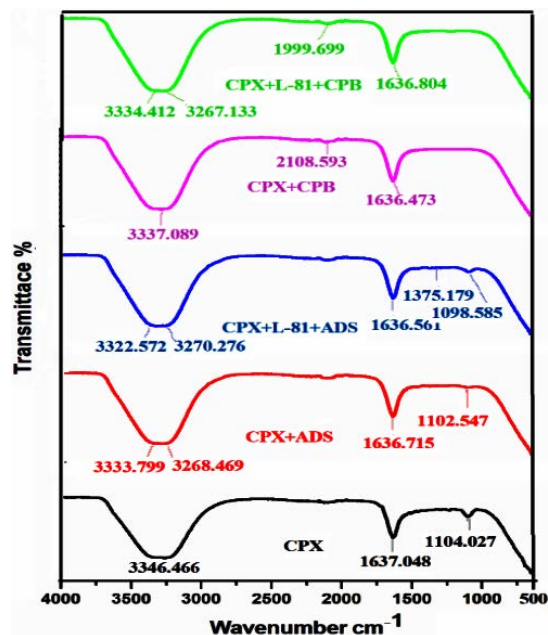
**Fig. 5. Absorbance CPX, CPX+ L-81+CPB with ethylene glycol as co-solvent.**

Infra-red studies

An infrared study helps to detect the structural changes occurring due to the addition of drugs to the mixed micellar system^{19,21,28-30}. In addition, it gives information about the proximity of one group to another.

In this experiment, we have carried out an IR study of five samples Fig. 6. The one with pure drug CPX alone displayed intense broadband at 3346 cm^{-1} , another one at 1637 cm^{-1} assigning for C=C stretching, and 1104 cm^{-1} for C-O-C stretching vibration. The one at 3346 cm^{-1} stands for OH stretching vibration with intermolecular bonding. It was seen to lower to 3333 cm^{-1} , 3337 cm^{-1} and 3334 cm^{-1} for the next four samples. Hence, there was no probable change at this site of the molecule. In the second band at 1637 cm^{-1} , the C=C stretching vibration for the CPX molecule was seen to be unaltered for all five samples. There was no major shift of the peaks. Hence, there is very little interaction in this area. The third band

which was a weak one at 1104 cm^{-1} stands for the C-O-C stretching vibrations. In addition to ADS and ADS-L-81 to CPX, there was a minimal observable change, to 1102 cm^{-1} and 1098 cm^{-1} . Hence, this part of the bonding was also not affected due to mixed micellization.

**Fig. 6. FTIR spectrum of CPX and CPX in different micellar systems**

For the CPX, ADS, and L-81 combination there appeared a band at 1375 cm^{-1} which is representative of OH bending vibration, and 2120 cm^{-1} occurring due to C=N stretching vibration. With CPX and CPB combination the C=N stretching vibration is seen at 2108 cm^{-1} which is shifted significantly to 1999 cm^{-1} for CPX, CPB, and L-81 mixture. This shift of peak towards lower wave number indicates that (a) the mass of the molecule is more for the product or compound (b) there is a probable increase in bond length arising from the changes of electronegativity created by the high molecular weight of CPB surfactant molecules present in the vicinity. Hence, it can be predicted that there is possible hydrogen bonding in this area. In CPX, CPB, L-81 combination the ethereal C-O-C bands have disappeared that means there is bonding in this area.

Conductometric study

Conductivity measurement is one of the most accurate ways to observe the micellization of ionic surfactants. Specific conductance of any

surfactant depends upon the formation of nature of ions after ionization, type of solvents, temperature, and addition of foreign substances. In this work, four sets of experiments were carried out to assess the electrochemical insight of drug-surfactant interactions. The electrical conductivity method has been utilized to observe the interaction as well as the association of different molecules in an aqueous medium³¹⁻³⁵.

Ionic surfactants behave as strong electrolytes and dissociate completely into their ion (Kohlrausch's law of independent mobility of ions) whereas at or after CMC, after aggregates are formed, the mobility of ions slows down. At concentrations above CMC, dissociation is somewhat weak because micelles are partially ionized. Hence, the electrical conductivity after CMC is fully dependent on the degree of micellar ionization^{36,37}.

There exists a balance of forces between the electrostatic repulsion of the negatively charged head group of ADS, positively charged one in CPB, and attractive forces of the alkyl chain lengths. These forces are reflected in the behavior of conductivity. Moreover, there is a substantial contribution of the existing micelles in solution towards the specific conductance at a given concentration. This micellar contribution is higher than that of the counter ions of the surfactant. Hence, it dominates in the display conductance measurement.

As observed from Table 7, there are two sets of solutions used (i) Anionic surfactant ADS was taken in different concentrations (ii) ADS-CPX was used and the conductance was measured. The concentrations were all above the CMC of ADS (CMC of ADS=6 mM). Hence, it is expected that the micellar contribution dominated over the counterion part. There was a gradual increase in conductance value with an increase in ADS concentration. This is because the tendency to aggregate increases with rising in the concentration of ADS.

Calibration of 0.1N KCl = 12.85 μs^{-1} , Cell constant = 1.00 cm^{-1} , Temperature = 25 K

Table 7: Specific conductance of an ionic surfactant ADS and ADS in presence of drug CPX

Sl. No	Concentration (mM)	CPX mL	ADS mL	Water mL	Conductance μs^{-1}
1	0.01	0	3.5	17.5	0.36
2	0.015	0	5.25	15.75	0.42
3	0.02	0	7	14	0.51
4	0.025	0	8.75	12.25	0.53
5	0.03	0	10.5	10.5	0.69
6	0.01	1	3.5	16.5	0.31
7	0.015	1	5.25	14.75	0.49
8	0.02	1	7	13	0.6
9	0.025	1	8.75	11.25	0.66
10	0.03	1	10.5	9.5	0.74

The value of conductance, therefore, increases from 0.36 to 0.69 μs^{-1} . In addition to the drug CPX to each of the above concentrations of ADS, there was also an increasing trend of conductance. This indicated the CPX-ADS complex had a higher conductance value compared with ADS alone (Fig. 7). The solution with high conductivity is expected to have a greater charge carrying capacity³⁸. With this property, they are probable to have a bigger particle size (CPX-ADS complex) than ADS alone. Compounds with large ions are expected to be more soluble than small ions in a high dielectric constant medium like water.

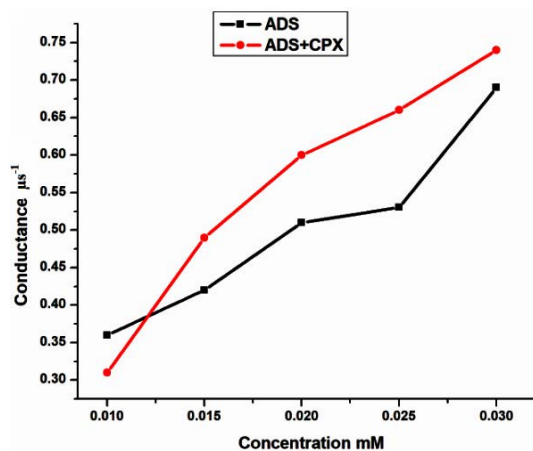


Fig. 7. Specific conductance of ADS and CPX +ADS

When the ion size is small, they are closer to each other in solution. Hence, they have strong attraction forces which are difficult to break by water molecules. So, they are less soluble. Large ion sizes however have the opposite trend. Hence, they are more soluble in the aqueous medium because they can break the bondings in water easily.

In Table 8 also there are two sets of experiments carried out. The first set with cationic surfactant CPB alone in different concentrations and the second one with CPB+CPX. Here also the conductance of the first set increases from 0.14 to 0.19 μs^{-1} whereas for the second set there is a small gradual increase from 0.20 to 0.22 μs^{-1} Fig. 8. This increase also follows the same trend as ADS which infers that there is an increase in insolubility.

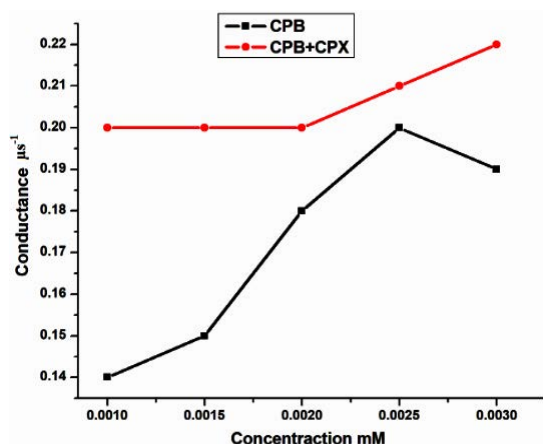


Fig. 8. Specific conductance of CPB and CPX+CPB

Table 8: Specific conductance of an ionic surfactant CPB and CPB in presence of drug CPX

Sl. No	Concentration (mM)	CPX mL	CPB mL	Water mL	Conductance μs^{-1}
1	0.001	0	0.42	20.58	0.14
2	0.0015	0	0.63	20.37	0.15
3	0.002	0	0.84	20.16	0.18
4	0.0025	0	1.05	19.95	0.2
5	0.003	0	1.26	18.74	0.19
6	0.001	1	0.42	19.58	0.2
7	0.0015	1	0.63	19.37	0.2
8	0.002	1	0.84	19.16	0.2
9	0.0025	1	1.05	18.95	0.21
10	0.003	1	1.26	17.74	0.22

It can therefore be concluded from conductivity studies that anionic surfactant has better solubilization capacity for the drug CPX compared to cationic surfactant CPB. Hence, the presence of ADS in a mixed micellar system helps to improve the solubilization of the drug. This is also corroborated by UV and co-solvent investigations.

CONCLUSION

The interaction of CPX with two mixed micellar systems, viz. Pluronic L81-ADS and PluronicL81-CPB were investigated. The solubilization of CPX was higher in L81-ADS compared to neat L81, ADS, and L81-CPB combinations. The mixed micelle of L81-CPB was less effective because of the hydrophobic nature o/f L-81; and probable cationic-cationic head group repulsion in the mixed micellar system. The solubilization was effectively higher in ethanol and ethylene glycol as co-solvent for both the mixed micellar systems. To conclude it can be said that anionic surfactant ADS can be used in the mixed micelle for enhanced solubility of CPX.

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Conflict of interest

The authors declare that they have no conflict of interest.

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