RSC Advances

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Journal:	*RSC Advances*
Manuscript ID:	RA-ART-03-2014-002177.R2
Article Type:	Paper
Date Submitted by the Author:	29-Apr-2014

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Drug – surfactant interaction: Thermo-acoustic investigation of sodium dodecyl sulfate and antimicrobial drug (Levofloxacin) for potential pharmaceutical application

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Abstract

In the present study, the advantages of surfactant micelles as vehicle are taken into consideration and the impact of potential antimicrobial drug (levofloxacin) on micellar system of anionic surfactant (SDS) has been studied. It would therefore be interesting to evaluate the region of micelle formation in order to design such system which could prove valuable in pharmaceutical formulations. In this context, conductance study, critical micelle concentration (CMC), standard thermodynamic parameters of micellization namely ΔH_m^o, ΔG_m^o and ΔS_m^o have been evaluated at four different temperatures (298.15 to 313.15) K. Molar volume and compressibility measurements have also been carried out to evaluate the apparent molar volume and apparent molar adiabatic compression of drug – surfactant complex and discussed in terms of the solute – solute and solute – solvent interactions. In addition spectroscopic analysis (FTIR and ^{1}H–NMR) confirmed the presence of intermolecular interaction between levofloxacin – SDS moiety within studied concentration. Conclusively, this study provides an indication to assess and develop surfactant immobilized levofloxacin for better biological action.

Key Words: Antimicrobial drug; Levofloxacin; SDS; Micellization; Interaction

Introduction

In recent years, the understanding of the mechanism of interaction between surfactant micelles and drugs are important to design drug formulations and delivery systems. Surfactant micelles are widely used in drug industry in order to enhance drug solubility, sustain drug stability, organize release of drug and drug uptake, moreover to improve bioavailability and biological profile of drugs.[1-3] Surfactants are also employed in many pharmaceutical formulations, such as suspensions or emulsions of water insoluble drugs, as solubilizers in injectables and moreover in medicated shampoos. Since both the surface activity and micellization have implications on the biological efficacy of many drugs, SDS is chosen for this study. Antimicrobial drugs, used worldwide contribute to one – fourth of all prescription and reports for half of the allocated drug budget in hospitals.[4] Fluoroquinolone antibiotics are an important class of antimicrobial agents which exhibit activity against a wide range of gram – positive and gram – negative microorganisms. Levofloxacin or L–ofloxacin, the bacteriologically active L–isomer of the racemic fluoroquinolone ofloxacin, is a broad spectrum antimicrobial agent, acts by inhibiting bacterial DNA gyrase which is required for DNA replication and thus causes bacterial lysis.[5] Levofloxacin shows potential activity on most strains of bacterial pathogens which are responsible for urinary tract, gastrointestinal and abdominal infections, including gram – negative and gram – positive for example *Escherichia coli*, *Haemophilus influenzae*, *Pseudomonas aeruginosa*, and methicillin – sensitive *Staphylococcus aureus*, *Enterococcus faecalis*, and *Streptococcus pyogenes* etc.[6,7]

Further, the release of poorly soluble drugs may be increased by the presence of surfactants, which may decrease the aggregation of drug particles and consequently, increase the area of the particles available for dissolution. The lowering of surface

tension may also be a factor in aiding the penetration of water into the drug mass. This wetting effect operates especially at low surfactant concentration; however above CMC, the increase in saturation solubility of the drug substance by solubilization in the surfactant micelles can result in more rapid rates of drug dissolution. This will increase the rate of drug entry into the blood stream and may affect peak blood levels. However, very high concentrations of surfactant may decrease drug absorption by decreasing the chemical potential of the drug. This results when the required surfactant concentration exceeds the amount affective to solubilize the drug.[8]

Numerous measurements, especially thermodynamic and spectroscopic play a significant role to understand the nature of molecular interactions in order to gain knowledge of drug action in surfactant micellar assembly. Sometimes drug conformation is affected by added these co – solutes due to solvent effects or their binding. The colloidal properties of drugs are largely determined by the nature of aromatic ring systems of their hydrophobic moieties and such drugs are useful in probing the relationship between molecular architecture and physico – chemical properties.[9] One important property of surfactants is the formation of colloidal – sized clusters in solutions known as micelles, which have particular significance in pharmaceutical technology because of their ability to act as vehicle and disperse bioactive molecules at the site of action.[10,11] In this context, we intend to evaluate critical micelle concentration (CMC), thermodynamic parameters of micellization of SDS along with compressibility studies in the presence of levofloxacin (hemihydrate) in aqueous solution at four different temperatures, in addition to spectroscopic studies likely, FTIR and ^{1}H NMR. These studies give insight with regard to intermolecular interaction of SDS-levofloxacin system. The study is of paramount importance as the drugs of fluoroquinolone class are showing resistance to microbes.

Materials and methods

Sodium dodecyl sulfate (SDS) of analytical grade (AR grade and mass fraction purity 0.99) was obtained from Merck Chemicals (India). Levofloxacin having (mass fraction purity 0.97) was obtained as gift sample from Glenmark Pharmaceutical Ltd, Baddi (Himachal Pradesh) India. Freshly prepared doubly distilled water was utilized, prepared from double distillation unit (HARCO & Co.) whose specific conductance and pH is in the range $\approx (1–4) \cdot 10^{-6}$ Scm^{-1} and 6.5–7.0 at 298.15 K, respectively. The complete concentration range (1–14 $mmol \cdot kg^{-1}$) has been selected for SDS to cover the region of micelle formation. Three different concentrations were fixed for levofloxacin i.e. 0.01, 0.05 and 0.10 M for conductance whereas density and ultrasonic velocity measurements have been carried out at only 0.01 and 0.05 M concentration of levofloxacin. FTIR and ^{1}H–NMR were performed at the highest concentration (levofloxacin 0.10 M). The chemical structures of levofloxacin and sodium dodecyl sulfate have been presented in Fig. 1.

Digital conductivity meter Cyber Scan CON–510 was used to obtain specific conductivity (κ). The calibration of conductivity cell was carried out with 0.01 M KCl (mass fraction purity 0.99) sample solution supplied by Merck chemicals. The temperature was maintained constant at ± 0.1 K by circulating water from thermostat through a double walled vessel containing the solution. The CMC data was further utilized in calculation of thermodynamic parameters. Density (ρ) and ultrasonic velocity (u) data for SDS solutions thus prepared were obtained with a high precision Anton Paar Density and Sound Analyzer (DSA–5000). The instrument was calibrated with de – ionized water obtained from a Millipore – Elix system whose conductivity, κ and the pH were well within the experimental range as mentioned

earlier. FTIR spectra were recorded at a frequency range of 4000–400 cm^{-1} using Shimadzu Infra Red Spectrometer, (model FTIR–8400S). Proton–NMR spectra of the compounds were recorded with Bruker Avance–II 400 NMR spectrometer operating at 400 MHz. The chemical shifts are reported in the δ scale in parts per million (ppm). Digital microscopic images were obtained by Motic Images Plus 2.0, Hong Kong.

Results and Discussion

Conductance and thermodynamic measurements

The CMC values correspond to a given additive content (levofloxacin) have been determined from the plots of specific conductance (κ) against surfactant concentration. The experimental points lay along two tangents on the obtained plot and the intersection being taken into consideration as the CMC value. The tangents were drawn addressing maximum points with higher regression value in pre - micellar and post micellar region. The Fig. 2 represents the plot of specific conductivity of SDS in presence of levofloxacin (0.01 M). In the presence of drug, the CMC values have been found to be lower in comparison to the standard value[12] of CMC of SDS in water as presented in Table 1. In present study, the CMC value of SDS in water was found to be 8.1 M at 298.15K which is agreement with literature.[12] The presence of different substitution (functional groups) on levofloxacin likely, -F- and -COOH- contributes eminently for better interaction and therefore causing earlier micellization. The extra hydrophobicity offered by levofloxacin seems to reduce CMC values of SDS. This decrease in CMC of SDS in aqueous solution of levofloxacin may also be attributed to the presence of hydrogen bonding between the –H (COOH) of the drug and the –O (SO_4) of the SDS moiety as well as the presence of hydrophobic interaction between the hydrophobic tail of the SDS and the hydrophobic group of the drug making

micellization prior to that occurs in case of water.[13] Thus, the combined effect of these two factors (hydrophobic interaction and H-bonding) dominates the ion – ion (–COO^- of drug and O^- of SDS) and ion – hydrophilic (–COO^- of drug and SO_4^{2-} of SDS) interaction occurs during the process of micellization. Also, there is an increase in CMC values with rise in temperature showing the constraint dehydration in the hydrophobic core which delays the micellization process. [14] This increase in CMC at higher temperature may also be due to the progressive disruption of water structure around the hydrophobic portion of the surfactant molecules that opposes the micelle formation leading to increase in CMC values. [15] In addition, the increase of temperature provides heat as a source of energy to increase the kinetics motion of the surfactant molecules and collisions cause less tendency of aggregation of the surfactant molecules to become micelles.

Before calculating the thermodynamic parameters of micellization, we intend to examine the temperature dependence of X_{CMC} (CMC expressed in mole fraction) of SDS in aqueous solution containing levofloxacin at each concentration. From the results and plots, it has been found that the X_{CMC} values of surfactant increases with increase in temperature but it decreases linearly with increase in levofloxacin concentration which is supported by our earlier studies with synthetic antioxidant.[16] The X_{CMC} data have been reported in Table 1 and was used to calculate various thermodynamic parameters of micellization such as standard enthalphy of micellization, ΔH_m^o standard entropy of micellization, ΔS_m^o and standard free energy of micellization, ΔG_m^o. The relations used for standard enthalpy change, standard entropy and Gibbs free energy change for micellization which are as follows[17,18]:

$$\Delta H_m^o = -RT^2(2-\alpha)[d(\ln X_{CMC})/dT] \quad (1)$$

$$\Delta S_m^o = \frac{\Delta H_m^o - \Delta G_m^o}{T} \quad (2)$$

$$\Delta G_m^o = (2-\alpha)RT\ln(X_{CMC}) \quad (3)$$

The $d(\ln X_{CMC}/dT)$ is the slope of the straight line obtained by plotting ln X_{CMC} against temperature, α = degree of counter ion dissociation which was calculated from the relation, $\alpha = S_2/S_1$, where, S_1 and S_2 are the slopes in the pre – and post – micellar regions. Thermodynamic parameters of micellization for SDS in different aqueous solutions of levofloxacin in the temperature ranging from (298.15 to 313.15) K have been reported in Table 2. The ΔH_m^o values have been found to be negative at all temperatures; moreover ΔH_m^o < 0 in all levofloxacin concentrations indicative of exothermic effect of surfactant. The value of ΔS_m^o is however, positive at all temperatures as well as at all concentrations of levofloxacin. These negative, ΔH_m^o and positive, ΔS_m^o values for these systems might be indicative of the contribution due to electrostatic interactions in addition to hydrophobic interaction. Negative values of ΔG_m^o suggested that the system is feasible with spontaneous micelle formation. In addition, the values of ΔG_m^o have been found in support of earlier studies on ionic surfactants in water.[19,20] The ΔG_m^o values have been found less negative at lower levofloxacin concentration and found to negatively increasing with increase in levofloxacin content in the mixture. Considering, ΔG_m^o with higher negative values, it is suggested that levofloxacin at 0.10 M solubilizes to greater extent; transfer from dispersed to micellar phase more readily. However with rise in temperature, ΔH_m^o values do not vary significantly suggesting that 'London dispersion' interactions

remain the main attractive force for micelle formation.[21] One of the main reasons for this formation is the attainment of minimum free energy state. The main driving force for the formation of micelles in the increase of entropy that occurs when the hydrophobic regions of the surfactant are removed from water and ordered structure of water molecules around this region of the molecules is lost.[22]

Volumetric and compressibility studies

The density, ρ and ultrasonic velocity, u data for SDS in 0.01 and 0.05 M levofloxacin have been reported in Table 3. The densities of solution in aqueous drug solutions increase with concentration of solute but decrease with temperature. The data have been used to calculate the apparent molar volume (V_ϕ) and apparent molar adiabatic compression (κ_ϕ) values over a wide concentration range of SDS, 1–14 M at different temperatures ranging from (298.15 to 313.15) K and have been calculated using the relation.[23-25]

$$V_\phi = \frac{M}{\rho} + \frac{[\rho_o - \rho]}{m\rho\rho_o} \tag{4}$$

$$\kappa_\phi = V_\phi\kappa_s + \frac{[\kappa_s - \kappa_o]}{m\rho_o} \tag{5}$$

where m (mol·kg^{-1}) is the molality of the solution, which was calculated from the molar concentration data using the relation: m = 1/[d/C–M/1000][26], here m (mol·kg^{-1}) stands for the molal concentration and M (g·mol^{-1}) for relative molar mass of SDS, ρ (kg·m^{-3}) is the density of the solution, ρ_o (kg·m^{-3}) is the density of the solvent system i.e. aqueous solution of the levofloxacin. κ_s (TPa^{-1}) and κ_o (TPa^{-1}) stands respectively for isentropic compressibility of the solution (aqueous solution of SDS in levofloxacin)

and solvent (aqueous solution of levofloxacin), respectively. The κ_s values were calculated as $\kappa_s = 1/\rho u^2$.[27] The decrease in κ_s values with increase in drug concentration signifies electrostatic effect of this drug on the surrounding medium and thus rendering the solution rather incompressible.[28] A similar behavior has also been found in case of aqueous drug – surfactant, protein – surfactant system.[29] Further insight into the type and extent of interaction of SDS in the presence of drug is obtained from the behavior of both V_ϕ and κ_ϕ. The variations of parameter with SDS have been shown in Fig. 3. and the values have been reported in Table 2. The V_ϕ values are positive at all temperatures and increases with rise in temperature. Fig. 3. describes the behavior of V_ϕ in case of SDS at 0.01 and 0.05 M levofloxacin. A pattern can be seen which has emerged from the V_ϕ results, represented in Fig. 3. that the graphs have a curved shape appearing at low – concentration region of the surfactant. Thereafter, the decrease in V_ϕ is almost linear as the surfactant concentration approaches the CMC. The results thus, imply that in the concentration region > 6 mmol·kg^{-1}, where V_ϕ values are practically independent of surfactant concentration can be attributed to micellization of SDS, but for concentration < 6 mM, where V_ϕ value decreases with the surfactant concentration can be attributed to the pre – micellar effect. This peculiar behavior of V_ϕ as a function of surfactant concentration is well established in the volumetric properties of the surfactant solutions.[30,31] Further amphoteric nature of drug result causes the decrease in electrostatic repulsion of SDS polar group through electrostatic interactions and enhancing the hydrophobic interaction of surfactant. It happens because, the electrostatic repulsion between surfactant anions decreases, and consequently, the added levofloxacin molecule decreases the thickness of solvation layer around negative

head group of SDS. Further, the data could not be analyzed in terms of limiting apparent molar volume (V_ϕ^o) and slope (S_v^*) values of the Masson's equation ($V_\phi = V_\phi^o + S_v^*\sqrt{m}$), for the reason that V_ϕ dependence on SDS has been found to be non – linear which is not a characteristic feature of electrolytic solutions.[32–34] However, an attempt is made to derive information as regard to drug – surfactant interactions from the dependence of V_ϕ on surfactant concentration. The values of κ_ϕ verses [SDS] shows the similar behavior as that of V_ϕ, thus supporting each other.

FTIR analysis

The FTIR analysis was undertaken to determine the information about the existing functional substitutions which can be considerably influenced by the available surrounding environment. Hence, FTIR study was used to analyze and gain structural information about the existing intermolecular interactions.[35] Interpretation of the structural changes has been carried out in terms of frequency shift and band width. The spectrum of levofloxacin showed prominent band at 3264 cm^{-1} corresponding to –COOH– group, in addition, the band at 3031 cm^{-1} (–CH– stretching), 1724 cm^{-1} (–C=O–), 1291 cm^{-1} (C–N), and 1085 cm^{-1} for fluorine, respectively as shown in Fig. 4(a). Fig. 4(b) represents the typical spectrum of SDS. The methylene anti – symmetric and symmetric vibrations were observed at 2957 cm^{-1}, 2851 cm^{-1}, and 2919 cm^{-1} for methylene anti – symmetric and symmetric stretching, and 1469 cm^{-1} for alkyl –CH– deformation, respectively. Spectrum of pure SDS depict bands at 1222 cm^{-1} and 1082 cm^{-1}, signifying –S=O (stretching) vibrational modes of sulphonic group of SDS. The band due to –S=O stretching vibrations in SDS shifted to 1226 cm^{-1} and 1089 cm^{-1} in presence of levofloxacin, in addition, –CH– vibrations shift was observed at 2931 cm^{-1}

and 2859 cm^{-1} as shown in Fig. 4(c). This kind of slight increment in band width moreover low frequency shifts certified that the available environment is tightly packed and hygroscopic, indicating intermolecular interactions and suggesting binding of levofloxacin drug with surfactant molecules.

^{1}H–NMR analysis

A solute can arrange itself in the micelle in different ways. It may be completely incorporated in the hydrophobic core or may penetrate up to a certain depth depending on the type and site of interaction. It can be adsorbed on the micellar surface or can selectively interact with the aliphatic or bulkier chain of surfactant with nature of existing substitutions on the moieties. To gain more understanding about the interactions, the provided picture represents the structural features and substitutions of anionic surfactant (SDS) (Fig. 5.). Proton nuclear magnetic resonance (^{1}H NMR) is one of the techniques to gain deeper insight on the micellar system in presence of different moieties.[36] Due to the precision of the NMR spectrometer, a change of ~ 0.01 ppm or greater is considered a significant change.

In the present study, NMR was recorded for levofloxacin, surfactant, both in the absence and presence of levofloxacin. The NMR spectrum of pure levofloxacin, SDS, and SDS in presence of levofloxacin is presented in Fig. 6. In first spectrum Fig. 6(a), characteristic peaks of levofloxacin were obtained. Two methyl groups were recorded at ~ 1.56 ppm and ~ 2.32 ppm. The peaks of aromatic protons were recorded in the region 4.3–4.8 ppm as singlet and a peak at ~ 15.2 ppm corresponds to –COOH– group of levofloxacin. On the other hand, pure SDS (Fig. 6(b)), methyl protons were recorded at ~ 0.89 ppm and the bulk protons resonated at ~ 1.29 ppm. The characteristic peaks of β–CH_2 and α–CH_2 resonated at ~ 1.57 ppm and ~ 3.84 ppm integrating 2 protons for

each, respectively. The presence of levofloxacin brought significant changes which are recorded and presented in terms of chemical shift of α–CH_2–, β –CH_2– and –$(CH_2)_9$– segments of SDS. This shifting towards downfield can be attributed to the deshielding effect created by fluorine present at levofloxacin. The α –CH_2– showed movement with a shift of ~ 0.02 ppm. The β –CH_2– and –$(CH_2)_9$– segments of SDS showed substantial movement of ~ 0.08 ppm and ~ 0.07 ppm, respectively, as shown in Fig. 6(c). However, –CH_3– was also observed with movement of ~ 0.08 ppm. This provides an assumption of existing intermolecular interaction.

Digital microscopic study

Most physical properties of molecules get modified by the interactions between colloidal spheres.[37] In order to gain more insight and understand the structural characterization, the microscopic visualization technique was opted in this present investigation. The samples includes SDS in the presence and absence of drug, were prepared via the process of lyophilization (freeze drying). All the samples were visualized under 10× and 40 × optical lenses as shown in Fig. 7. A hint of binding of levofloxacin with SDS molecule can be visualized in the obtained sample of SDS with drug [Fig.7 (e, f)]. The presence of drug molecule over SDS aggregation was observed. Thus, the visualization stands as a parallel study depicting some kind of drug–surfactant interaction. Moreover, this technique allowed us to collect some drug-surfactant binding information. It is also proposed that the study does not provide the locus of drug molecule within surfactant structural arrangement and for this some better technique are suggested likely, atomic force microscopy or steady state and time-resolved fluorescence technique.

Conclusion

With regard to aggregation behavior of the system, it is well understood that levofloxacin and SDS is an ideal system. The decrease in CMC in the presence of levofloxacin is due to the establishment of additional hydrophobic interactions between hydrophobic parts of surfactant and levofloxacin. Thermodynamic parameters revealed that the system is feasible and there is spontaneous formation of micelles. From spectroscopic studies, intermolecular interactions were observed. In addition, ^{1}H–NMR spectroscopy also revealed intermolecular interaction existence. Microscopic technique provided the visual feature of the mixture, utilized in the study. Therefore, we conclude that more insight in this area of subject can lead to design better bio – effective systems from pharmaceutical point of view.

Acknowledgement

Author V. Bhardwaj and P. Sharma would like to thank DST, New Delhi for financial grant (Ref. No. SR/FT/CS-59/2009), K. Sharma thanks UGC, New Delhi for the award of Basic Scientific Research Fellowship (No. F. 7–75/2007(BSR)). The authors would also like to thank SAIF department – Panjab University, Chandigarh, for providing spectral data and Glenmark Pharmaceutical Ltd., Baddi, Solan (Himachal Pradesh) India, for providing levofloxacin as gift sample.

Declaration

Authors declare no conflict of interest.

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Fig. Captions

Fig. 1. Chemical structures of (a) levofloxacin and (b) sodium dodecyl sulfate (SDS).

Fig. 2. Specific conductance of SDS in aqueous solutions containing levofloxacin; a) 0.01M, b) 0.05M, c) 0.10M at four different temperatures [298.15 (■), 303.15 (●), 308.15 (▲), and 313.15 (▼)] K.

Fig. 3. Plot of apparent molar volume (V_ϕ) for 0.01 M: ■ and 0.05 M: ● levofloxacin/ M at 298.15 K.

Fig. 4. FTIR spectrum of (a) Levofloxacin, (b) SDS, and (c) SDS in presence of levofloxacin.

Fig. 5. Structural features and substitutions of SDS.

Fig. 6. ^{1}H-NMR spectrum of (a) Levofloxacin, (b) SDS, and (c) SDS in presence of levofloxacin.

Fig. 7. Digital microscopy images (a) SDS at 10×, (b) SDS at 40×, (c) Levofloxacin at 10×, (d) Levofloxacin at 40×, (e) Levofloxacin-SDS at 10×, and (f) Levofloxacin-SDS at 40×; (Concentration used; SDS 9 mM and levofloxacin 0.10 M).

Table 1. CMC, X_{CMC}, α and standard thermodynamic parameters of micellization of SDS in aqueous solutions containing levofloxacin at four different temperatures ranging from (298.15 to 313.15) K

T/K	*CMC*	$X_{CMC}\cdot 10^4$	α	ΔH_m^o / kJ·mol^{-1}	ΔG_m^o / kJ·mol^{-1}	ΔS_m^o / J·K^{-1}·mol^{-1})
SDS (control)						
298.15	8.1×10^{-3}	1.46	0.402	-7.08	-25.85	63.00
303.15	8.2×10^{-3}	1.48	0.425	-7.21	-25.86	61.57
308.15	8.5×10^{-3}	1.53	0.439	-7.38	-25.90	60.11
313.15	8.8×10^{-3}	1.58	0.465	-7.50	-25.76	58.35
Levofloxacin (M = 370.38 g·mol^{-1}) m_A = 0.01 M						
298.15	7.5×10^{-3}	1.35	0.687	-8.72	-28.98	67.98
303.15	7.8×10^{-3}	1.40	0.655	-9.23	-30.05	68.69
308.15	7.9×10^{-3}	1.42	0.621	-9.78	-31.25	69.68
313.15	8.0×10^{-3}	1.44	0.596	-10.29	-32.29	70.30
Levofloxacin (M = 370.38 g·mol^{-1}) m_A = 0.05 M						
298.15	7.0×10^{-3}	1.25	0.635	-9.07	-30.36	71.47
303.15	7.3×10^{-3}	1.31	0.612	-9.53	-31.25	71.69
308.15	7.6×10^{-3}	1.36	0.588	-10.02	-32.18	71.93
313.15	7.9×10^{-3}	1.42	0.569	-10.49	-32.95	71.77
Levofloxacin (M = 370.38 g·mol^{-1}) $1.35m_A$ = 0.10 M						
298.15	6.9×10^{-3}	1.24	0.584	-9.40	-31.53	74.26
303.15	7.1×10^{-3}	1.27	0.566	-9.85	-32.40	74.43
308.15	7.4×10^{-3}	1.33	0.542	-10.34	-33.30	75.52
313.15	7.8×10^{-3}	1.40	0.514	-10.89	-34.30	74.78

The estimated uncertainties for specific conductance is $2\cdot 10^{-6}$ cm^{-1} and ± 0.2 kJ·mol^{-1} for ΔH_m^o, ± 0.1 kJ·mol^{-1} for ΔG_m^o and ± 2.0 JK^{-1}· mol^{-1} in case of ΔS_m^o.

Table 2. Densities, ρ, ultrasonic velocity, *u,* isentropic compressibility, κ_s , apparent molar volumes, V_ϕ and apparent molar adiabatic compression, κ_ϕ of SDS in aqueous solutions of levofloxacin over the temperature range (298.15 to 313.15) K

$m \cdot 10^3$ / M	ρ / Kg·m^{-3}	u / m·s^{-1}	κ_s / TPa^{-1}	$V_\phi \cdot 10^4$ / m^3·mol^{-1}	$\kappa_\phi \cdot 10^2$ / m^3·mol^{-1}TPa^{-1}	ρ / Kg·m^{-3}	u / m·s^{-1}	κ_s / TPa^{-1}	$V_\phi \cdot 10^4$ / m^3·mol^{-1}	$\kappa_\phi \cdot 10^2$ / m^3·mol^{-1}TPa^{-1}
	Levofloxacin (M = 370.38 g·mol^{-1})									
	m^b = 0.01 M									
	***T/K* = 298.15**					***T/K* = 303.15**				
2	998.399	1498.24	446.20	2.78	16.38	996.958	1510.07	439.87	2.91	29.79
4	998.467	1498.33	446.12	2.66	11.77	997.024	1510.56	439.56	2.73	12.63
6	998.522	1498.55	445.96	2.65	9.13	997.091	1510.79	439.40	2.67	9.43
8	998.589	1498.88	445.74	2.62	6.85	997.134	1511.10	439.20	2.68	7.51
10	998.669	1499.10	445.57	2.6	6.03	997.205	1511.16	439.13	2.65	7.57
12	998.701	1499.27	445.46	2.62	6.08	997.270	1511.25	439.05	2.63	7.51
14	998.792	1499.44	445.31	2.59	5.74	997.322	1511.27	439.02	2.63	7.83
	***T/K* = 308.15**					***T/K* = 313.15**				
2	995.284	1520.83	434.40	3.11	21.07	993.371	1529.97	430.05	3.50	22.44
4	995.352	1521.03	434.26	2.83	12.46	993.446	1530.08	429.96	3.01	14.27
6	995.409	1521.32	434.07	2.76	8.89	993.497	1530.27	429.83	2.89	11.13
8	995.477	1521.56	433.90	2.71	7.35	993.552	1530.45	429.71	2.82	9.60
10	995.539	1521.56	433.87	2.68	7.85	993.603	1530.43	429.69	2.79	9.84
12	995.583	1521.60	433.83	2.68	8.12	993.685	1530.47	429.64	2.74	9.49
14	995.637	1521.57	433.83	2.67	8.54	993.734	1530.45	429.63	2.73	9.69

	Levofloxacin (M = 370.38 g·mol^{-1}) m_A = 0.05 M									
	T/K = 298.15					*T/K* = 303.15				
2	1003.390	1502.26	441.61	3.42	77.69	1001.968	1512.02	436.55	3.18	135.11
4	1003.476	1502.30	441.55	2.93	42.72	1002.014	1512.42	436.30	2.91	67.07
6	1003.518	1502.57	441.37	2.84	29.45	1002.081	1512.69	436.11	2.79	45.33
8	1003.601	1502.90	441.14	2.75	21.93	1002.130	1513.04	435.89	2.75	34.08
10	1003.680	1502.08	441.59	2.69	24.20	1002.197	1513.12	435.81	2.71	28.73
12	1003.731	1502.30	441.44	2.68	20.83	1002.262	1513.24	435.72	2.68	24.98
14	1003.802	1502.45	441.32	2.66	18.59	1002.325	1513.30	435.65	2.67	22.57
	T/K = 308.15					*T/K* = 313.15				
2	1000.280	1522.81	431.11	3.19	118.54	998.375	1530.99	427.33	3.31	131.99
4	1000.346	1522.99	430.98	2.87	61.51	998.450	1531.11	427.23	2.91	68.88
6	1000.399	1523.30	430.78	2.79	41.46	998.508	1531.27	427.12	2.81	47.71
8	1000.482	1523.47	430.65	2.71	32.10	998.565	1531.35	427.05	2.75	37.70
10	1000.545	1524.58	429.99	2.68	21.33	998.615	1531.40	427.00	2.73	31.91
12	1000.584	1524.65	429.94	2.68	19.24	998.679	1531.45	426.94	2.70	27.96
14	1000.652	1524.70	429.88	2.66	17.64	998.734	1531.55	426.86	2.69	24.99

$m_{B,}$ is the molality of SDS in aqueous solution of levofloxacin, $m_{A,}$ is the molality of levofloxacin in distilled water. Standard uncertainties in ρ, u and T/K are ± $2 \cdot 10^{-3}$ kg.m^{-3}, ± 0.1 m·s^{-1} and 0.1 K. The experimental uncertainties calculate for V_ϕ and for κ_ϕ have been comes out to be ± $0.18 \cdot 10^{4}$ m^3·mol^{-1} and $0.05 \cdot 10^{2}$ m^3·mol^{-1}·TPa^{-1} respectively.

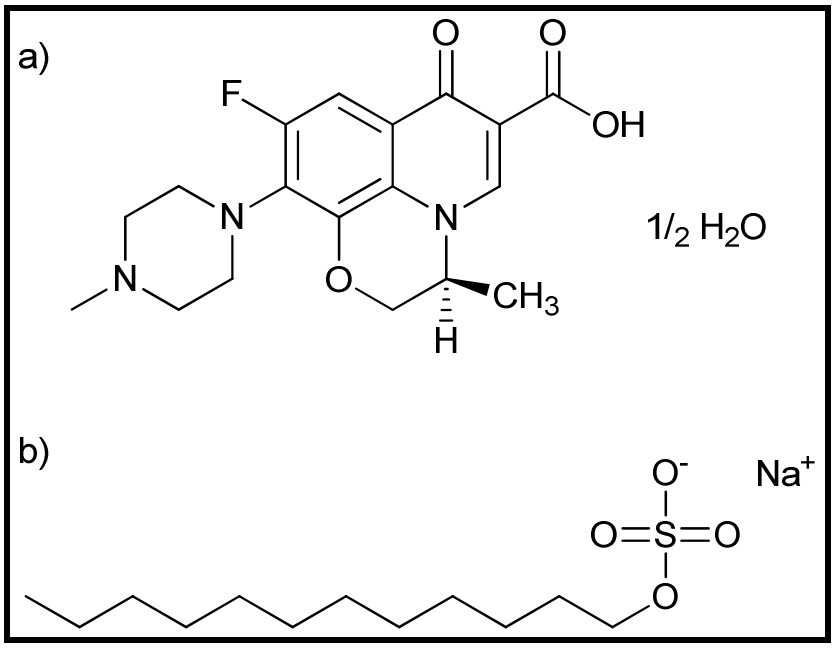


Fig. 1. Chemical structures of (a) levofloxacin and (b) sodium dodecyl sulfate (SDS).

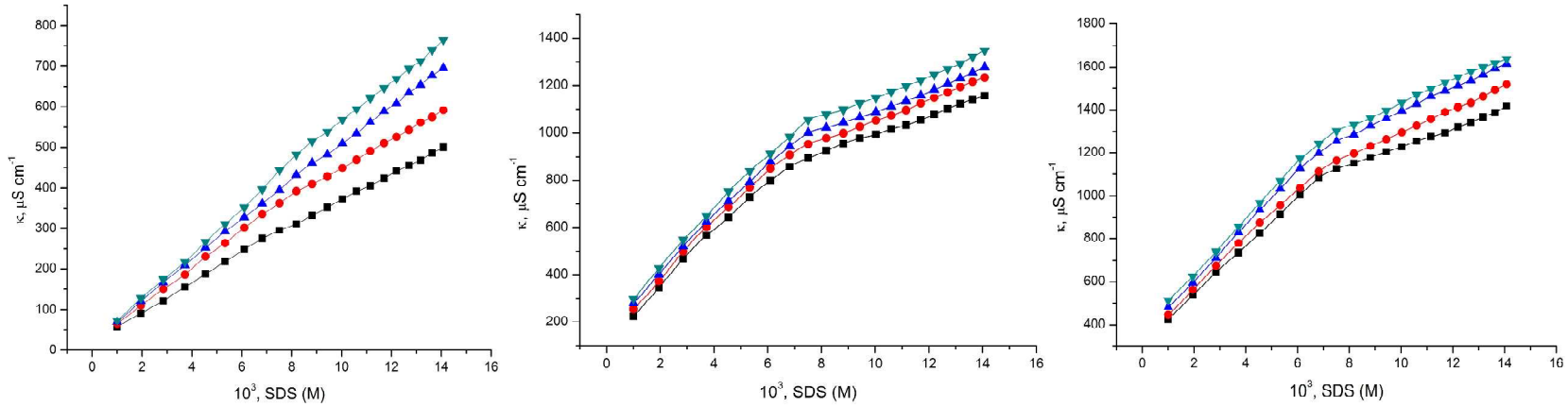


Fig. 2. Specific conductance of SDS in aqueous solutions containing levofloxacin; a) 0.01M, b) 0.05M, c) 0.10M at four different temperatures [298.15 (■), 303.15 (●), 308.15 (▲), and 313.15 (▼)] K.

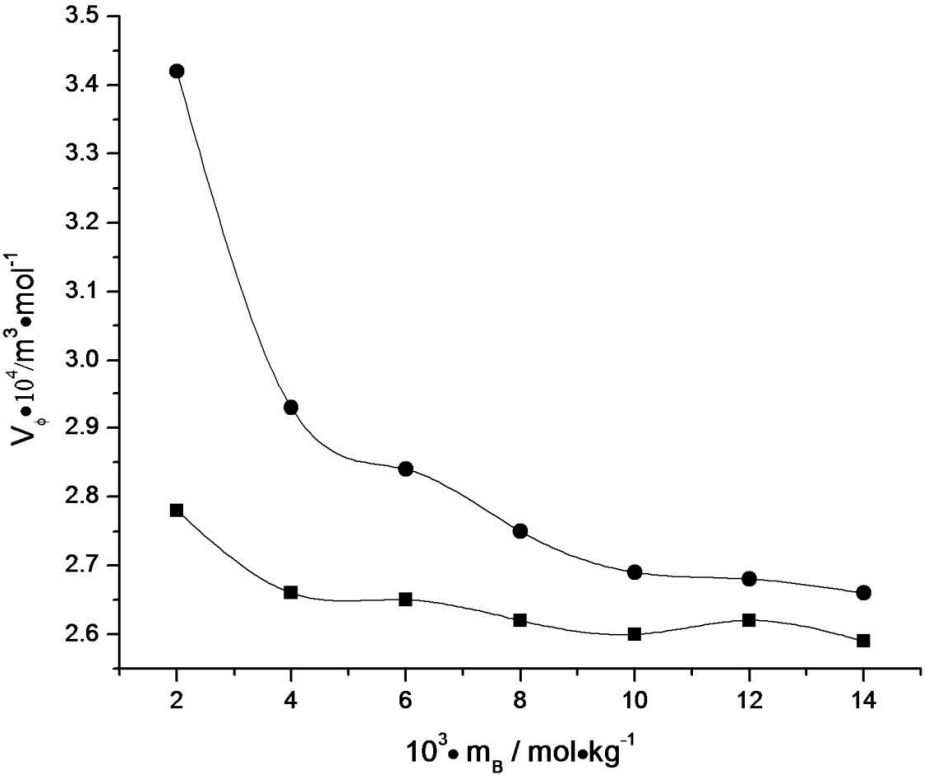
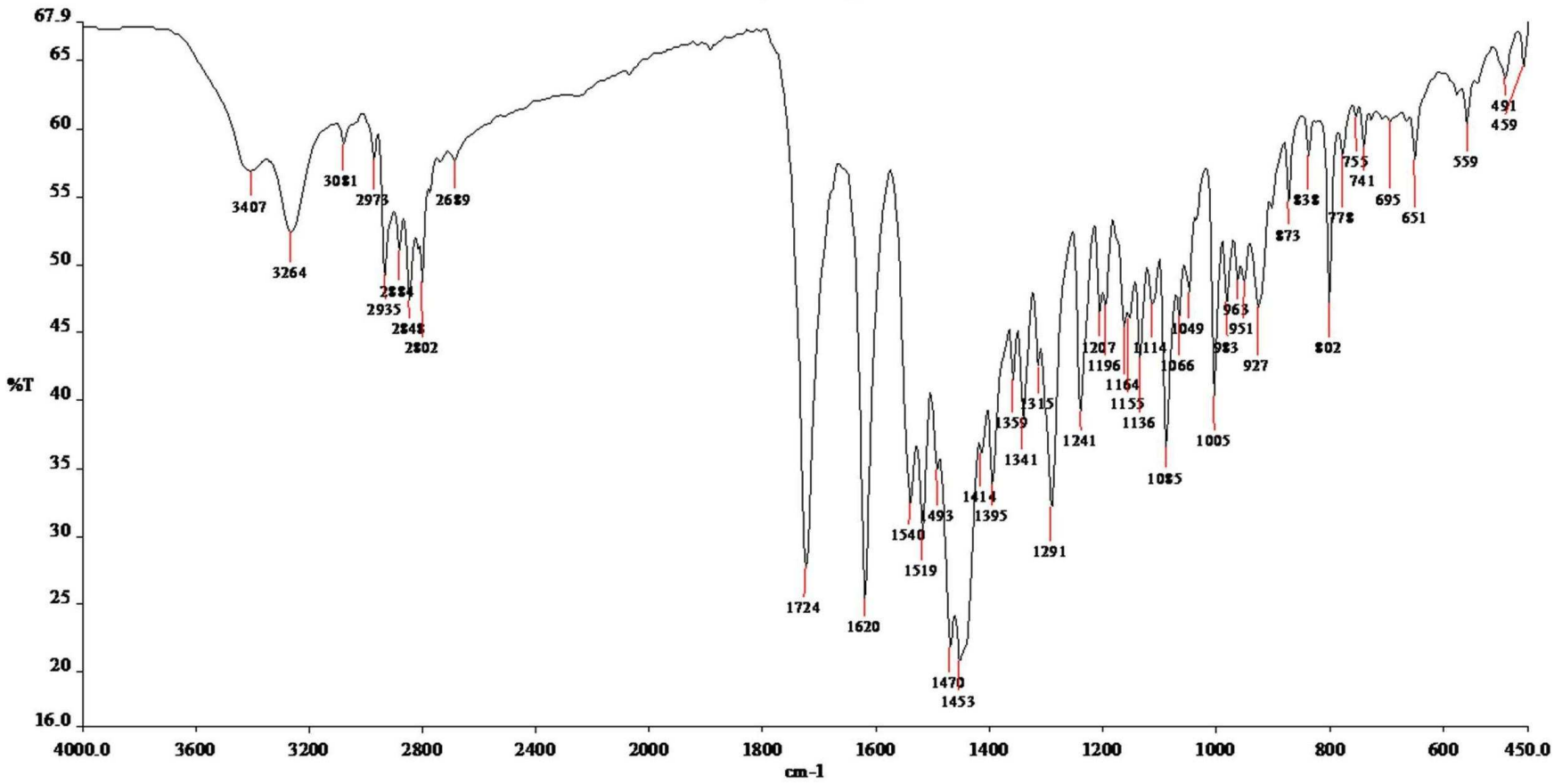


Fig. 3. Plot of apparent molar volume (V_ϕ) for 0.01 mol·kg^{-1}: ■ and 0.05 mol·kg^{-1}: ● levofloxacin/mol·kg^{-1} at 298.15 K.


%T
cm-1
3407
3264
3081
2973
2935
2689
1724
1620
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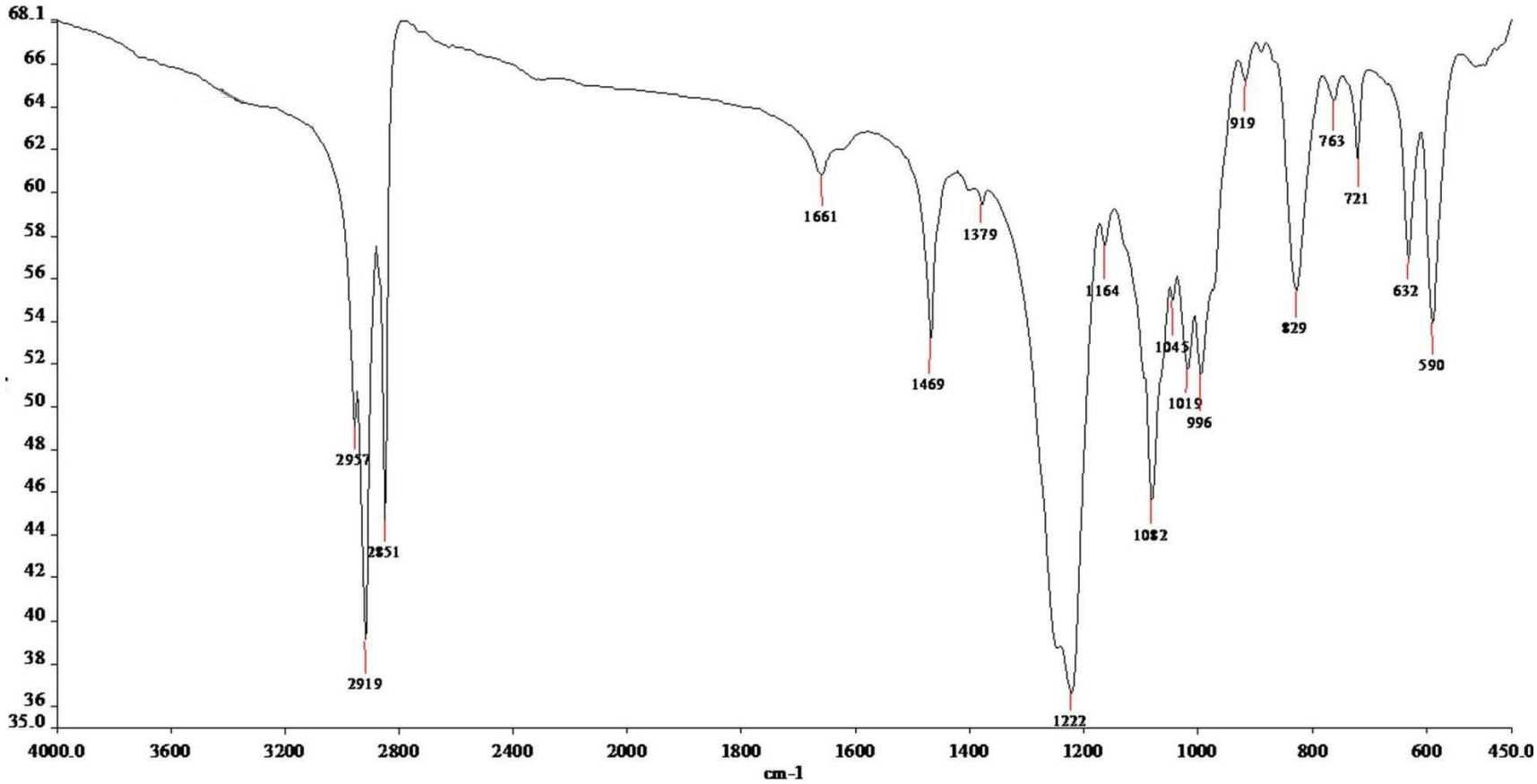
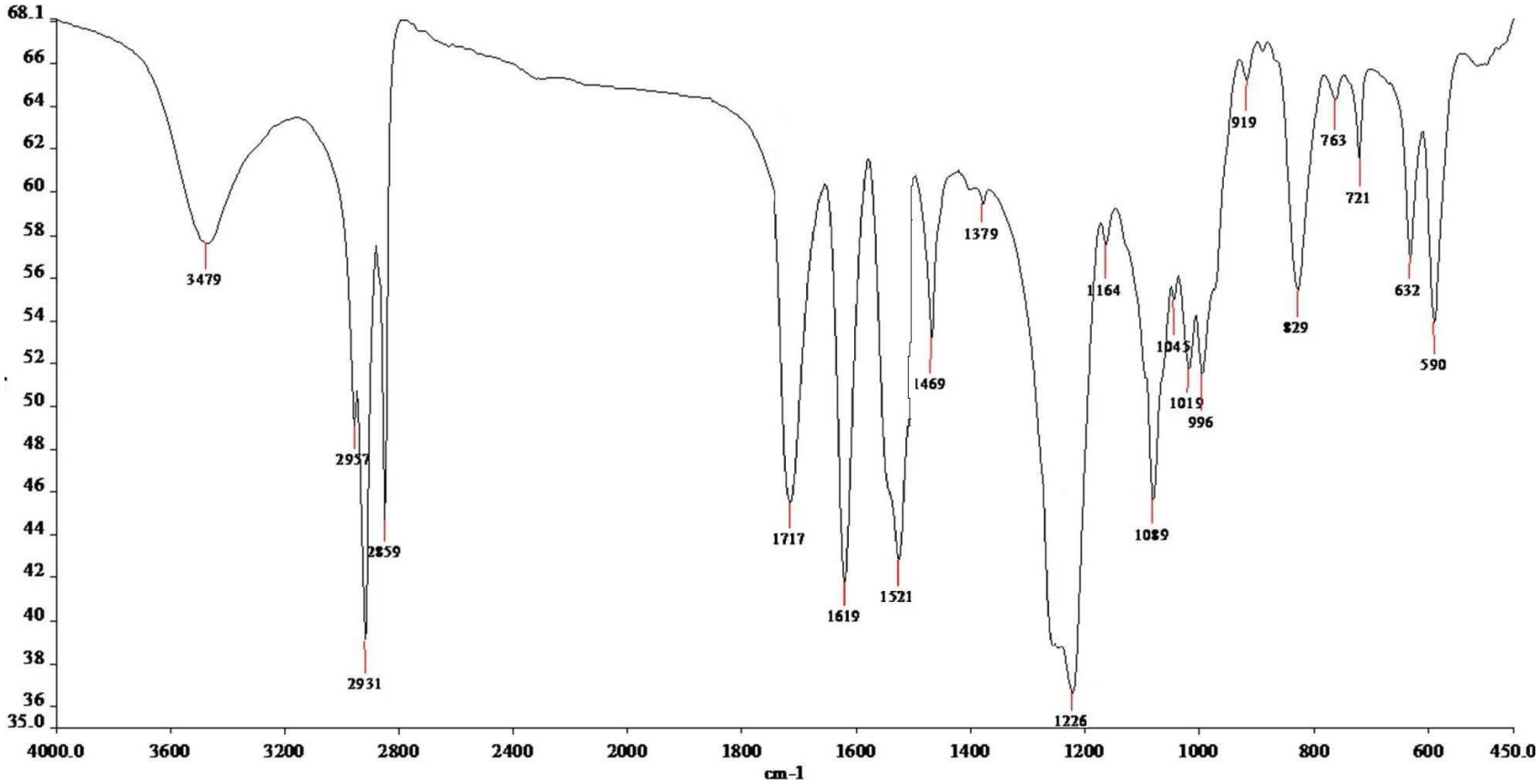
1519
1493
1470
1453
1414
1395
1359
1341
1315
1291
1241
1207
1196
1164
1155
1136
1114
1085
1066
1049
1005
983
963
951
927
873
838
802
778
755
741
695
651
559
491
459

(a)


68.1
66
64
62
60
58
56
54
52
50
48
46
44
42
40
38
36
35.0
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
450.0
cm-1
2957
2919
2851
1661
1469
1379
1222
1164
1082
1045
1019
996
919
829
763
721
632
590

(b)



(c)

Fig.4. FTIR spectrum of (a) Levofloxacin, (b) SDS, and (c) SDS in presence of levofloxacin.

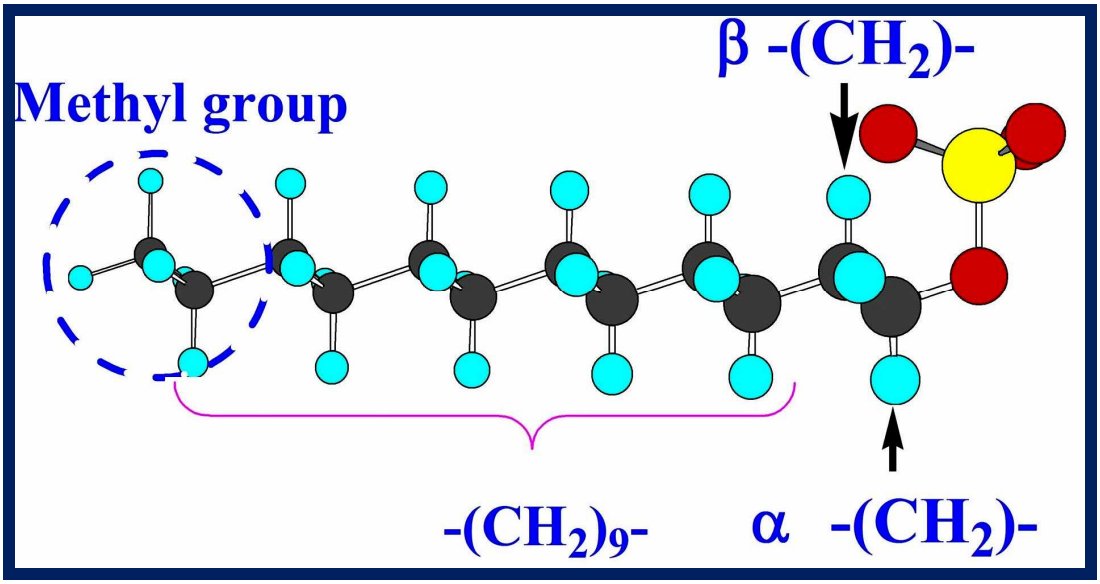
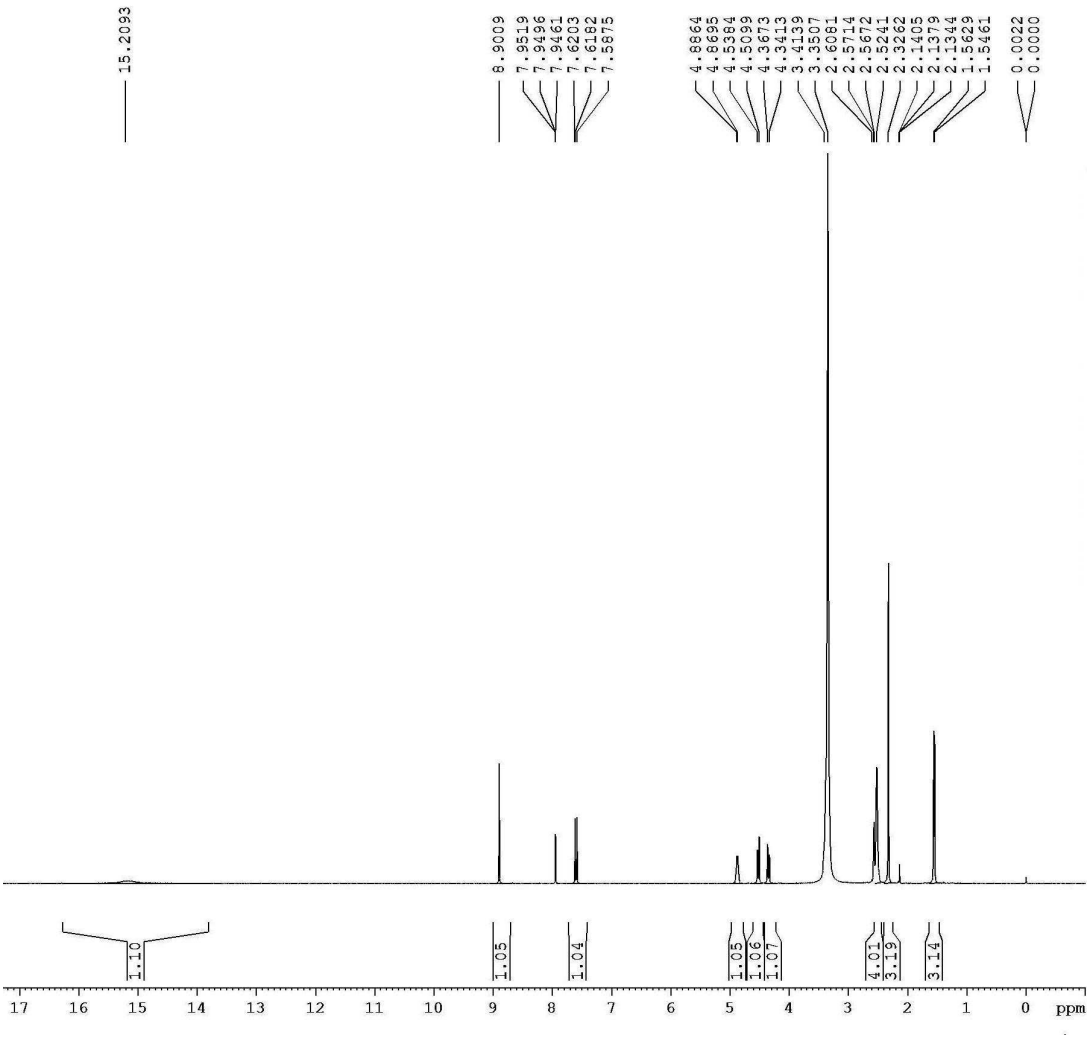


Fig. 5. Structural features and substitutions of SDS.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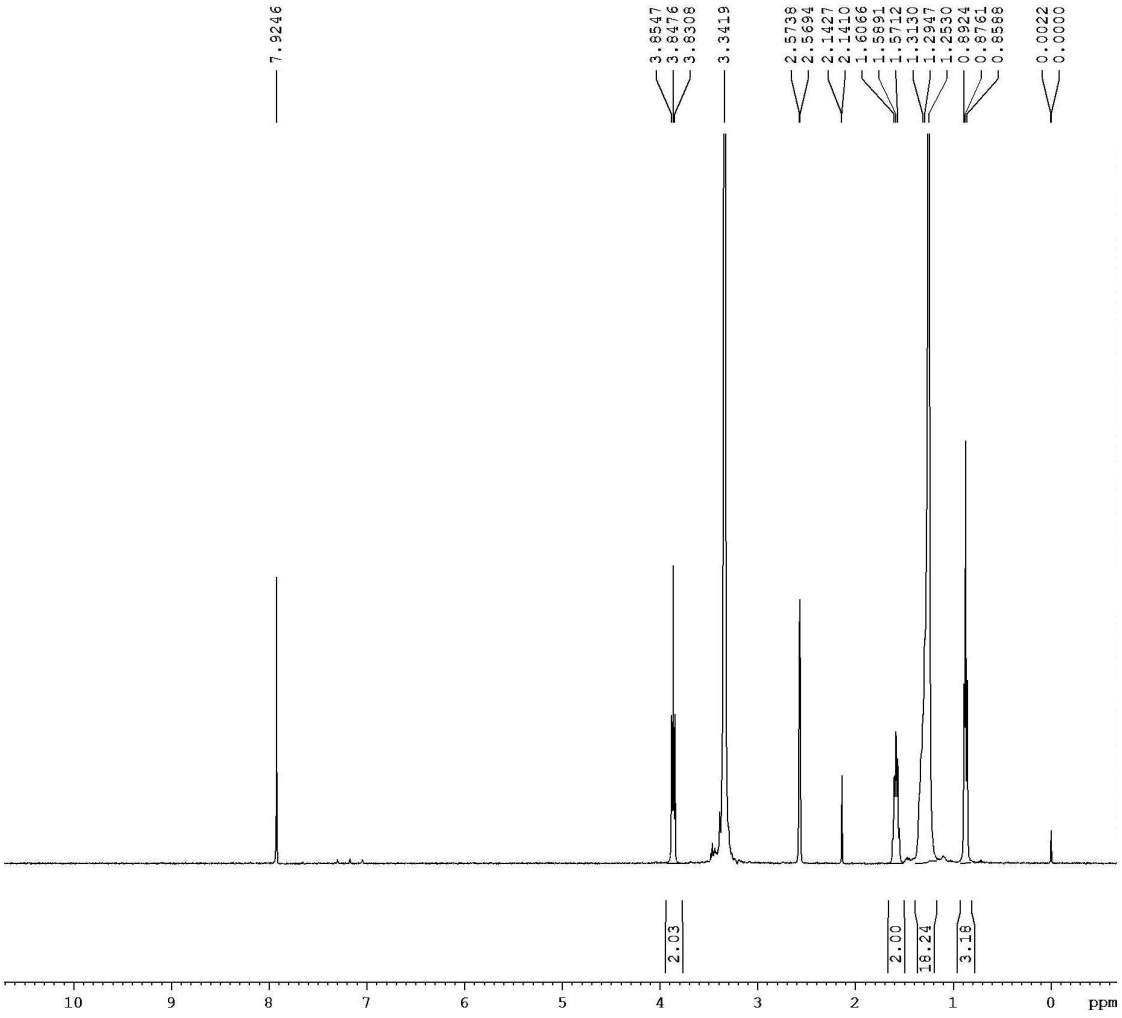
7.9519
7.9496
7.9461
7.6203
7.6182
7.5875
4.8864
4.8695
4.5384
4.5099
4.3673
4.3413
3.4139
3.3507
2.6081
2.5714
2.5672
2.5241
2.3252
2.1405
2.1379
2.1344
1.5629
1.5461
0.0022
0.0000
1.10
1.05
1.04
1.05
1.06
1.07
4.01
3.19
3.14
17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm

(a)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3.8547
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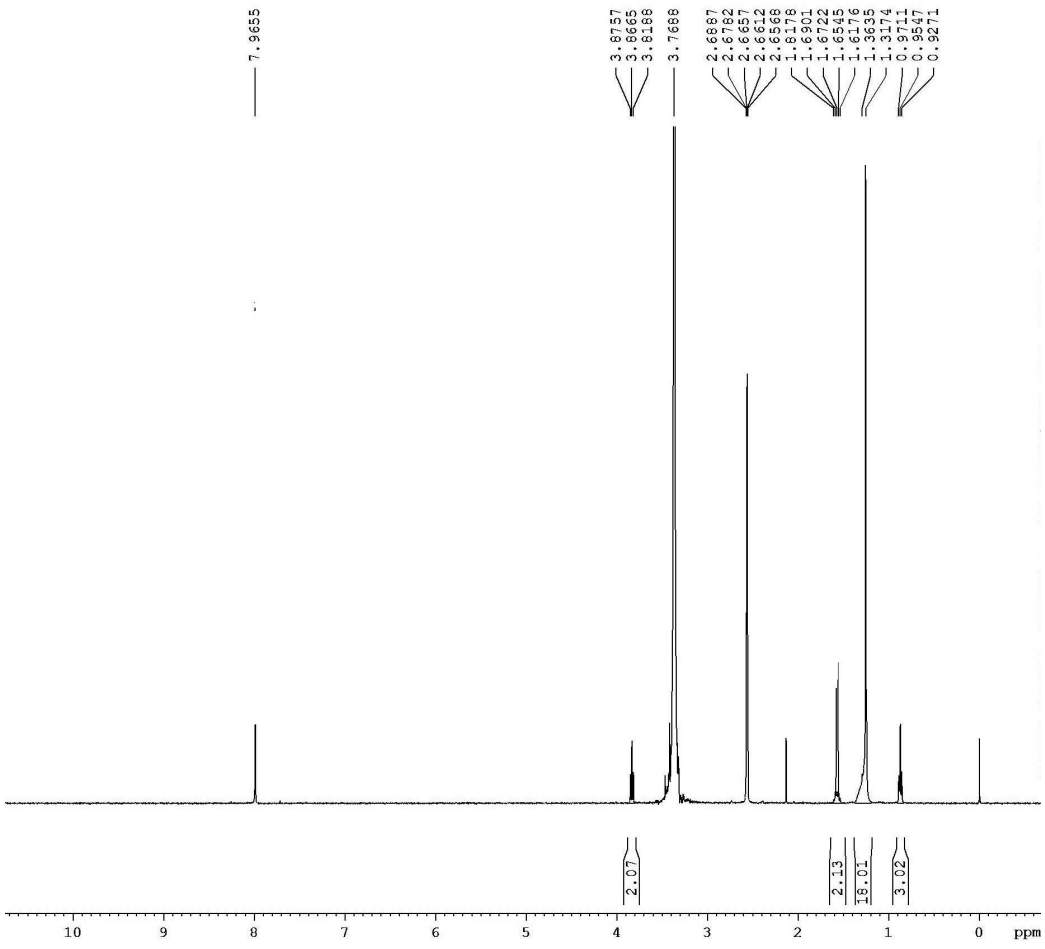
3.8308
3.3419
2.5738
2.5694
2.1427
2.1410
1.6066
1.5891
1.5712
1.3130
1.2947
1.2530
0.8924
0.8761
0.8588
0.0022
0.0000
2.03
2.00
18.24
3.18
10
9
8
7
6
5
4
3
2
1
0
ppm

(b)



(c)

Fig. 6. ^{1}H-NMR spectrum of (a) Levofloxacin, (b) SDS, and (c) SDS in presence of levofloxacin.

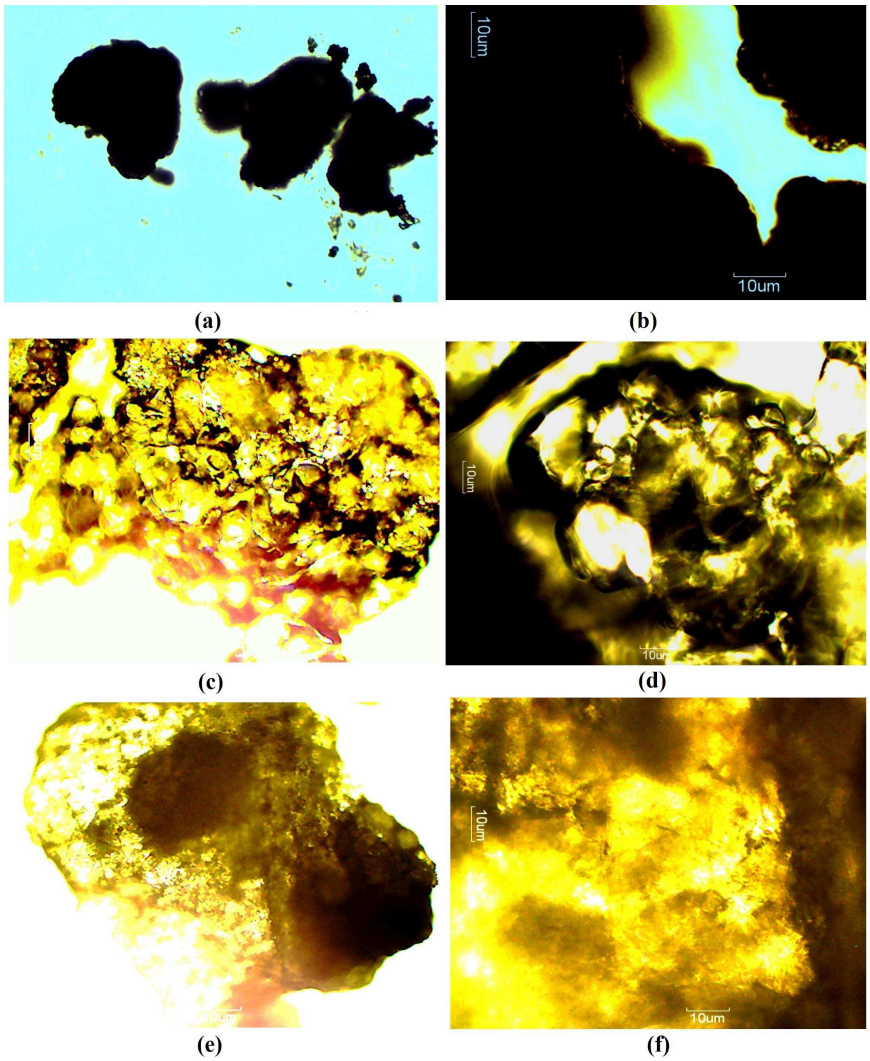


Fig. 7. Digital microscopy images (a) SDS at 10×, (b) SDS at 40×, (c) Levofloxacin at 10×, (d) Levofloxacin at 40×, (e) Levofloxacin-SDS at 10×, and (f) Levofloxacin-SDS at 40×; (Concentration used; SDS 9 mM and levofloxacin 0.10 M).

Graphical abstract