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RESEARCH ARTICLE

Spectrophotometric Determination of Loratadine in Syrup and Study Viscosity Conductivity and Thermodynamic of Binary Mixed Systems of Surfactants with Loratadine"

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Abstract

A simple, rapid and highly accurate UV spectrophotometric and one viscosity and conductivity methods for estimation of Loratadine in bulk and its pharmaceutical preparation. The method based on using direct ultraviolet detection on the wavelength range 190-400 nm. An absorption maximum was found to be at 286 nm. The percentage recovery of Loratadine ranged from 100.113 to 99.564 % in pharmaceutical syrup form. The developed method was validated with respect to linearity, accuracy (recovery), precision, limit of detection (LOD), limit of quantitation (LOQ), Sandell's sensitivity, molar absorbtivity, molar extinction coefficient and specificity. Beer's law was obeyed in the concentration range of 5-35 µg/mL having line equation y = 0.0248x+ 0.0621 with correlation coefficient of 0.9988.Then studied the factors affecting the formation of wormlike micelles through focusing of different concentrations of Lor. 100-1000 $\mu g.ml^{-1}$ in different temperatures (298.15, 303.15, 308.15 and 313.15 K) and at ratios of (20/80, 30/70 and 40/60).Thermodynamic functions (ΔG^o, ΔH^o, ΔS^o) were calculated for the process of micelles formation in the presence of Lor., the results indicated that the cationic (CTAB) and anionic (SDS) surfactants revealed a big tendency towards formation of wormlike micelles in Lor. Because intermolecular interactions. The other aspect included The prepared mixtures of surfactants have been study electrochemically using conductometric measurements in the aim of obtaining a relationship between conductivity ($L(\mu S.cm^{-1})$) and viscosity (η (pa.s)) of these solutions, but there is no linear relationship has been achieved.

Keywords: *Loratadine, Surfactant, Viscosity and conductivity.*

Introduction

Loratadine is a derivative of azatadine and a second-generation histamine H_1 receptor antagonist used in the treatment of allergic rhinitis and urticaria. Unlike most classical antihistamines (histamine H_1 antagonists) it lacks central nervous system depressing effects such as drowsiness. IUPAC Name ethyl 4-(13-chloro-4-azatricyclo [9.4.0.0(3, 8)] pentadeca-1(11), 3, 5, 7, 12, 14-hexaen-2-ylidne) piperidine-1-carboxylate.Its molecular formula is $C_{22}H_{23}C_lN_2O_2$ with molecular weight 382.9. The chemical structure is [1]:

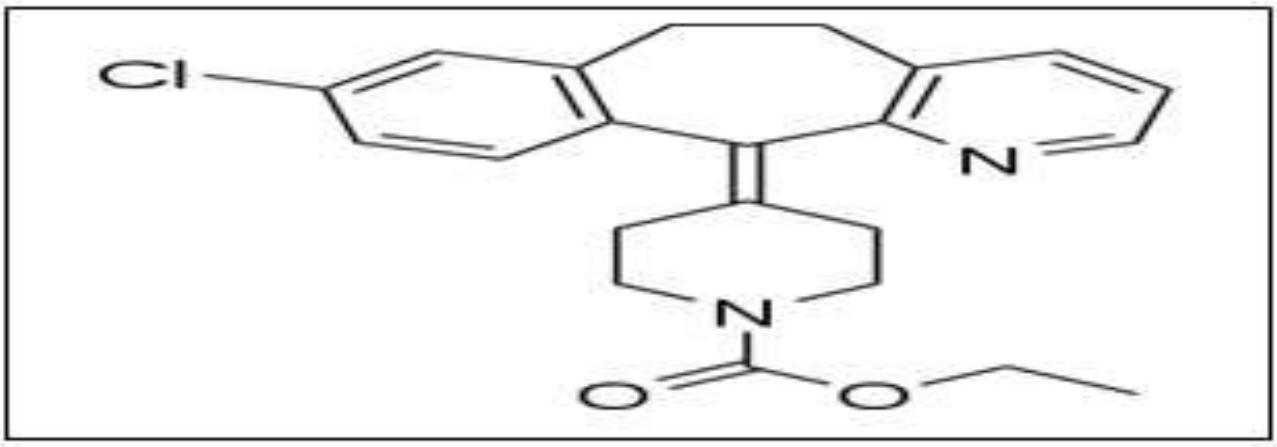

Figure 1: Chemical structure of Loratadine

Several analytical methods have been proposed for determination of Loratadine in pure and its pharmaceutical formulations These methods including UV [2, 3], Visible spectrophotometry [4], chromatography [5, 7], Titrimetry [8], Voltammetry [9], Potentiometry [10]. The surfactant compound is the material that works on remove or reduces surface tension between two non-matrices phases some of them are easier to mix by removal the surface tension between them. That surfactants play a major role in many applications as they are used as a cover to improve surface wetting and emulsification factors to increase the stability of emulsifiers and detergents to increase cleaning efficiency, as well as used in cosmetic and pharmaceutical industry [11, 12].

"When enough surfactant is dissolved in the water, many of the properties of the solution will change significantly, especially the surface tension which will decrease and the solubility of the solution to dissolve the hydrocarbons, these changes occur only when we reach a concentration greater than the specific concentration of this concentration called the concentration micelles critical (cmc) [13].An increase in viscosity means the growth of micelles because the viscosity is a positive indicator to be the micelles, Assemblies consisting of self-assembly of surfactants are called micelles, The process of forming the micelles is irreversible process and therefore is considered to be a dynamic structure [14], When increasing the concentrations of surfactants and electrolytes or without increasing the concentration of electrolytes, the micelles grow and increase, the self-assembly of the surfactant in the aqueous solution in various forms including spherical, wormlike, depending on the molecular structure, the temperature and the accompanying ion [15]. There are a number of published books, journals and research on micelles and their structures and thermodynamic composition [16, 18].

$$\frac{\eta_1}{\eta_2} = \frac{\sigma_1 t_1}{\sigma_2 t_2}$$

Where (t) is the time (min), ∂ (kg.m^{-3}) is the density

Chemicals and Standard Solutions

The chemicals used were of analytical grade, the SDI Samarra-Iraq furnished a Lor., methanol from Merk-Germany, SDS and CTAP from Fluka, pharmaceutical preparation (LORATEN (5mg/5ml)) from Haryana-India.

- The standard solution of Lor. 1000µg/ml was prepared by dissolving accurately weight 0.1gm of pure material in 10ml methanol and the volume was complete to 100ml with distilled water , from this standard solution 10 ml was transferred to 100 ml volumetric flask, and volume was made up-to the mark with 1:10 methanol: distal water to obtain standard solution of 100µg/ml.
- A series volumes of pharmaceutical preparation solution (LORATEN; 50µg/ml) 1-7 ml were put in a series of 10 ml calibrated volumetric flasks made up-to the mark with 1:10 methanol :distilled water.
- The standard solution of SDS (or CTAB) was prepared by dissolving accurately 2% wt of pure material in distilled water and completes the volume to 250ml in volumetric flask with same solvent [1].

The Aim of Project

UV spectrophotometric determination of Loratadine and study rheological properties effect of mixture the SDS and CTAB on the Loratadine and understanding the molecular interactions.

Experimental

Instrumentation

A Shimadzu UV-Visible-1650-Japan double beam spectrophotometer with 1cm matched quartz cells was used for all spectral measurements. The conductivity measurement (WTW), CD-2005 with an accuracy ±0.01 µs. cm^{-1}. Shaking water bath (K-GEMMY-ycw-012s-Taiwan). Viscosity for the solutions under study was measured through calculating the flow time by using Ostwald viscometer, which measures the flow time of the solution. Calculated of dynamic viscosity (η pas. s) from equation (1).

(1)

Procedure

It was include two parts:

First: A liquots volumes of standard Lor. Solution 0.5-3.5 ml; 100µg/ml were put in a series of 10 ml calibrated volumetric flasks. The absorbance was measured at 286 nm against a suitable blank. Hence 286nm was selected as λmax for analysis.

Second: Different solutions of a mixture of sodium Dodecyl sulphonate and cetayl tri-ammonium bromide were prepared in the presence of Lor. Standard solution and concentrations ranging from 10-100µg/ml and at temperatures (298.15, 303.15, 308.15 and 313.15 K).The required sample weight at each concentration was transferred into volumetric flask (10 ml) in order to run the required measurements.

Results and Discussion

Accuracy and Precision

The accuracy and precision of method were tested according to ICH [25], since the recovery percentage (Rec %) and relative standard deviation (RSD %) values were 100.113-99.564% and 0.902-0.457% respectively. These values reveled to good accuracy and precision".

LOD & LOQ

The Minimum concentration level at which the analyte can be reliable detected (LOD) & quantified (LOQ) were found to be 1.324 & 4.413 µg/ml respectively.

The Absorption Spectrum

The absorption spectrum of Loratadine shown in Figure 2. It gave maximum absorbance at 286 nm against suitable blank.

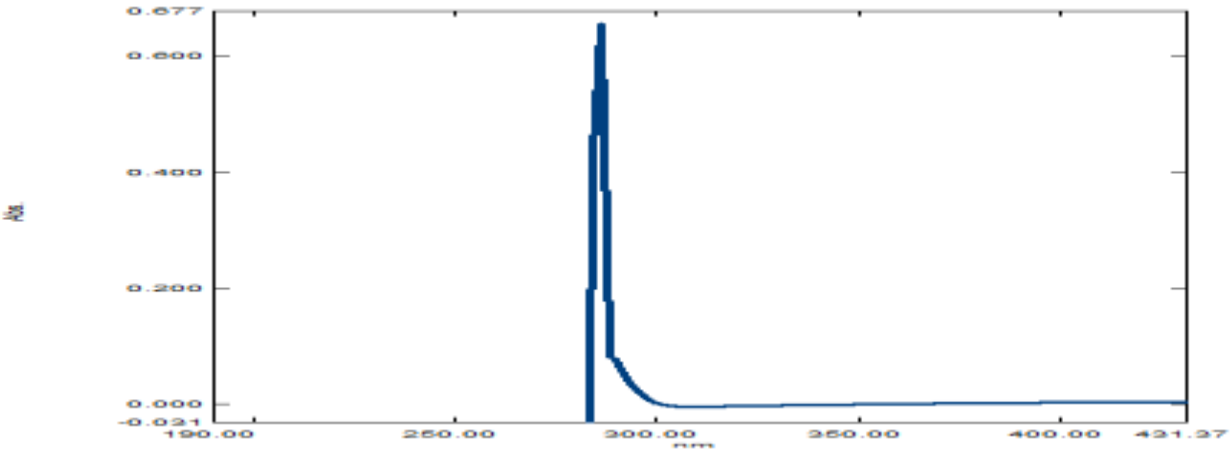

Figure 2: the absorption spectrum of Loratadine

Calibration Curve

The calibration curve of Lor. Showed good linearity at concentration up to 5-35 µg/ml The Molar absorptive, Sandell's index, R^2 were 9495.92 $L.mol^{-1}.cm^{-1}$, 0.0403 $\mu g.cm^{-2}$ and 0.9988 respectively with a straight line equation y = 0.0248x + 0.0621."The calibration curve shown in Figure 3 and the optical characteristics were shown in the Table 1.

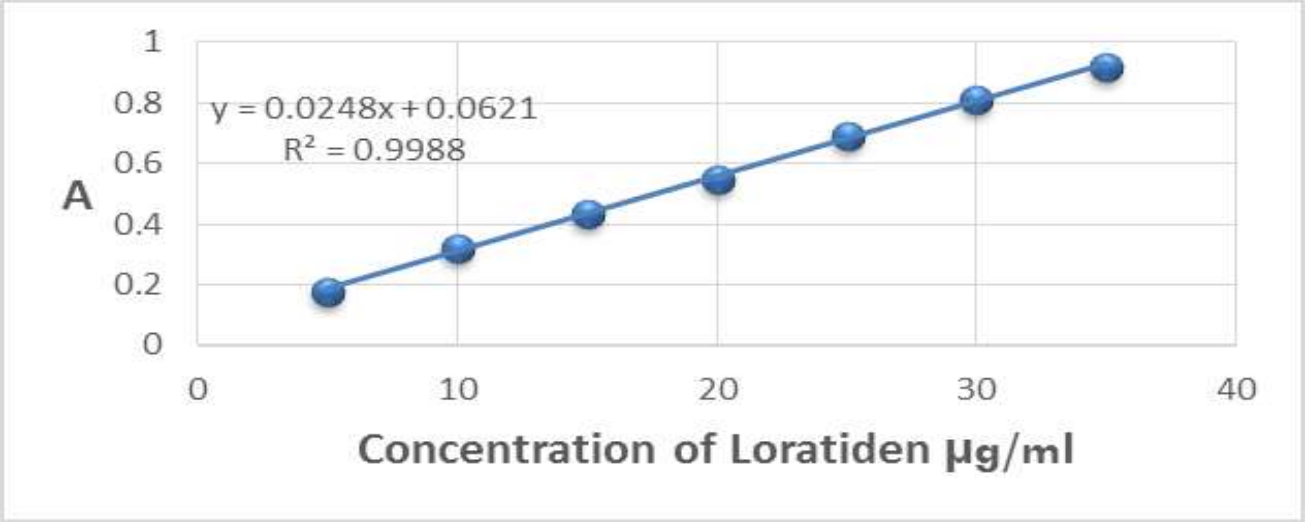

Figure 3: Calibration curve of Loratiden

Table 1: The optical characteristics of Loratadine

Method	λ_{max}(nm)	Linearity (µg.ml^{-1})	L.O.D (µg.ml^{-1})	L.O.Q (µg.ml^{-1})	Sandell's index (µg.cm^{-2})	Straight line equation	R^2
Suggested method	286	5-35	1.324	4.413	0.0403	y = 0.0248x + 0.0621	0.9988

Method Application

Two methods were used in the determination of Lor. in pharmaceutical preparation. There are:

Direct Method

An accurately volume 3, 5 ml from LORATEN; 50µg/ml were transferred into volumetric flasks, dissolved in 1:10 ml methanol: distilled water and complete to the mark with the same solvent. The proposed method was successfully applied for the determination of Loratadine in syrup. The values of the Rec. % and RSD% are summarized in Table 2. These values indicate that the proposed method have high accuracy and precision.

Standard Additions Method

The drug has been estimate in pharmaceutical preparation (LORATEN; 50µg/ml) by standard additions method, as curve shown in Figure 4.

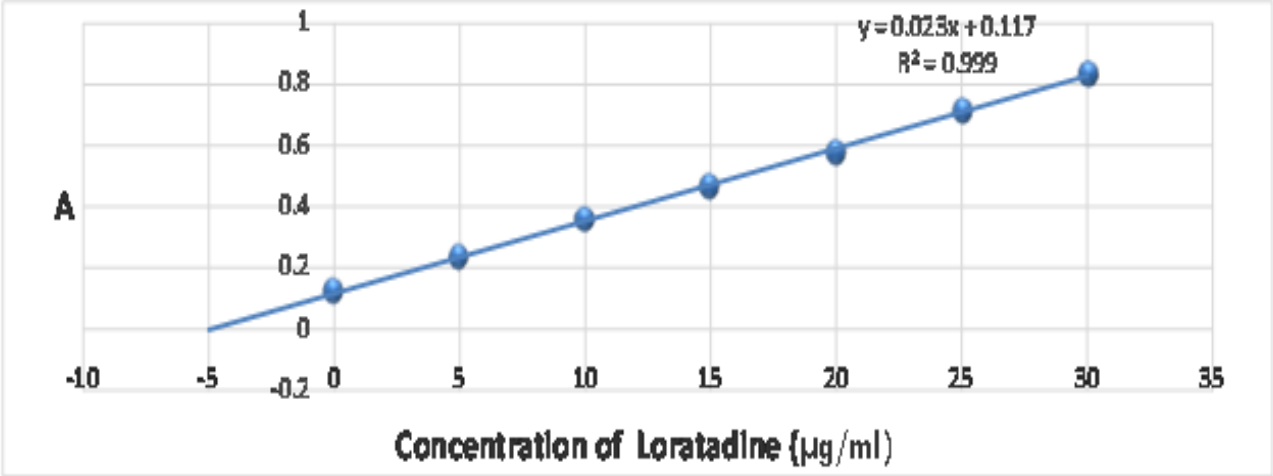

Figure 4: Standard additions curve

Table 2: Determination of Loratadine in LORATEN (5mg/5ml) syrup by spectrophotometric method

Direct method	Pharmaceutical	Taken (µg.ml^{-1})	Found (µg.ml^{-1})	Rec%	RSD % *
	LORATEN (syrup) 5mg/5ml	15	15.017	100.113	0.902
		25	24.891	99.564	0.457
Standard addition method		15	14.697	99.784	0.514
		25	25.069	100.278	0. 863

* Six replicate samples of pharmaceutical

Viscosity, Conductivity and Thermodynamic Measurement

"The effect of ratio mixture on the viscosity of the Loratadine and anionic SDS (Lor./SDS), Loratadine and cationic CTAB (Lor./CTAB) and Lor. / SDS: CTAB at different temperatures has been studied. the results show that the mixture of Lor/SDS:CTAB shows a high dynamic viscosity (η) peak at the ratio of 20/80,30/70 and 40/60 it was found that the viscosity was increased in the presence of Loratadine using at different consternation (100-1000 µg.ml^{-1}), leading to the growth of micelles [9] as illustrated clearly in Table"(3).

The viscosity was calculated by measuring the time of descent of the pure water and the time of descent and the density of the solutions of the surfactants at different temperatures required. Where η1, t1, σ1 represents the density, the time of descent and the viscosity of pure water respectively, while η2, t2, σ2 represents the density, the decay time and the viscosity of the surfactants solutions to be measured respectively.

The results in Table (3) indicate an increase in the viscosity values of the Lor./SDS:CTAB mixture. Especially in the mixing ratio

20/80,30/70 and 40/60 at 298.15K, compared with Lor./SDS, Lor./ CTAB, because the low temperature leads to the process of forming the micelles by providing kinetic energy that increases the possibility of the possibility of overlap Lor./SDS:CTAB. Due to interaction and molecular forces. Increasing the temperature, however, increases the kinetic energy of the molecules of surfactant, making it difficult to assemble and form the micelles.

Also, the results from Table (3) show that the viscosity values of the Lor.: SDS/CTAB mix increase irregularly with the increased concentration of Lor. This is due to the fact that Lor. This material has a high molecular weight and will work on the formation of wormlike micelles with the presence of SDS / CTAB due to the formation of strong electrostatic forces between the groups of heads with opposite charges as well as the hydrophobic effect of water to the hydrocarbon tail groups.

The mixture of the surfactant anion sodium dodecyl sulfonate SDS with the cation CTAB showed an increase in the dynamic viscosity curve and the ratio of 20/80 refers to the formation of wormlike micelles, high viscosity for zero-shear viscosity, at 20/80 Lor/CTAB the growth of micelles in solutions with more CTAB content and less SDS content, due to the tail group in the CTAB contains 16 carbon atoms, while the SDS contains 12 carbon atoms"[17, 20].

Since the cmc decreases with the length of the tail length, the process of formation micelles in the CTAB is faster than the SDS. Therefore, we observe the shift of the curve peak toward the greater content of the CTAB. As a result of the formation of strong electrostatic attraction forces between the groups of the heads of the opposite charge, then increasing the concentration of SDS and decreasing the concentration of CTAB will approach an area that is equal to that of SDS and CTAB where viscosity is less than before. That the increased concentration of SDS means higher cmc due to lower tail length when compared with CTAB and therefore a greater concentration of CTAB is needed to maintain the formation of wormlike micelles.

Therefore, increased SDS concentration and decreased CTAB concentration will result in decay and the transition to small micelles again, causing a decrease in the viscosity of the solutions until reaching the final solutions with high content of the SDS and the appearance of spherical solids again. This shows the importance of the tail group in the process of the formation of the wormlike micelles along with strong electrostatic attraction forces between the group heads of wormlike micelles, and that these results match what has been studied recently [17].

The results also show that the nature of the surfactants plays a large role in the formation of the micelles, such as the presence of the co-ions with the two surfactant, CTAB bromide and SDS sulfite, as well as the hydrophobic effect. The thermodynamic characteristics of the Lor..: SDS/CTAB mixtures were evaluated and the results were well correlated with the rheological changes of the mix. In order to calculate the thermodynamic properties of the Lor./ SDS: CTAB mixers and include the free energy (ΔG^o), enthalpy (ΔH^o) and entropy (ΔS^o) for the formation of micelles, these thermodynamic variables was estimated using the following equations [20, 21, 22]:

$$\Delta G = -RT \ln (\eta / 2*10^{-3}) \ldots\ldots\ldots\ldots\ldots\ldots (1)$$

$$D(\ln \eta / 2*10^{-3})/d(1/T) = -\Delta H^O/R \quad \ldots\ldots\ldots\ldots (2)$$

$$\Delta S^\circ = \frac{\Delta H^\circ - \Delta G^\circ}{T} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (3)$$

(R) is the gas constant, and (T) the absolute temperature. The relationship between ln η and inverted temperature 1 / T is drawn to extract the ΔH^o value of the inclination, note that a change in the enthalpy sign indicates that the process of emulation is exothermic process. "A negative ΔG indicates that the process is spontaneous, and that ΔS is negative because the randomization process is random, as shown in Table 6. The electrical conductivity of the prepared solutions for the exploration of the presence of wormlike micelles was studied. Wormlike micelles in order to obtain a relationship between this physical property and viscosity of these solutions as shown in Table 4.It is

noted from the results that increasing the temperature lead to a decrease in the specific conductivity may be because the increase in temperature higher than the temperature of Kraft with certain limits lead to increased composition of micelles and a decrease in the concentration of free particles. Since the viscosity of the solutions was good with Lor. This leads to the formation of wormlike micelles. This has contributed to maintaining the three solutions of 20/80, 30/70 and 40/60, which contain different concentrations of Lor. To show that the specific conductivity values are low for the strength of the molecular interactions, ie, they have little kinetic energy when they are alone without any addition, and there is no linear relationship between the viscosity and the specific conductivity, as shown in Figure"5.

Table 3: Viscosity values and other related thermodynamic functions for SDS/CTAB mixed system in Lor. At different temperatures

Lor. Conc. (µg.ml-1)	*η (Pa.s) x 10²(ΔG° kJ.mol⁻¹){ΔS° J.mol⁻¹.K⁻¹ }*				*ΔH° kJ.mol⁻¹*
	298.15K	**303.15K**	**308.15K**	**313.15K**	
	Ratio 20/80				
0*	2.9128 (-6.5283) {-233.042}	2.0035 (-5.7120) {-231.891}	1.2449 (-4.6085) {-231.710}	0.6647 (-3.076) {-232.904}	-76.010
100	3.1113 (-6.6889) -214.204	2.1291 (-5.8627) -213.399	1.3162 (-4.7488) { -213.549}	0.8002 (-3.5522) {-213.960}	-70.554
250	3.6671 (-7.0895) { -230.482}	2.5782 (-6.3371) {-229.163}	1.4783 (-5.0416) { -229.651}	0.8982 (-3.8482) {-229.793}	-75.808
500	4.5540 (-7.6174) {-264.068}	3.7853 (-7.2891) {-260.794}	1.9786 (-5.776) {-261.457}	0.9678 (-4.0394) {-262.845}	-86.349
750	5.7123 (-8.1698) {-272.450}	3.9221 (-7.3771) {-270.569}	2.2228 (-6.0696) {-270.045}	1.0051 (-4.1363) {-271.479}	-89.400
1000	6.0096 (-8.2934) {-268.757}	4.7893 (-7.8722) {-265.710}	2.3898 (-6.252) {-266.655}	1.1259 (-4.4271) {-268.242]	-88.427

Lor. Conc. (µg.ml-1)	*η (Pa.s) x 10²(ΔG° kJ.mol⁻¹){ΔS° J.mol⁻¹.K⁻¹ }*				*ΔH° kJ.mol⁻¹*
	298.15K	**303.15K**	**308.15K**	**313.15K**	
	Ratio 30/70				
0*	1.3592 (-4.6705) {-217.826}	1.0083 (-4.0099) {-216.117}	0.6320 (-2.8998) {-216.502}	0.3546 (-1.4671) {-217.620}	-69.615
100	1.8096 (-5.3681) {-244.994}	1.1201 (-4.2706) {-240.953}	0.6996 (-3.1560) {-240.678}	0.3887 (-1.7023) {-241.458}	-77.315
250	2.8999 (-6.5174) {-310.659}	1.2318 (-4.5062) {-312.182}	0.8002 (-3.4946) {-310.387}	0.3991 (-1.7700) {-265.783}	-99.144
500	3.5570 (-7.0152) {-288.898}	1.8787 (-5.5525) {-288.965}	0.8888 (-3.7592) {-290.118}	0.6119 (-2.8649) {-288.328}	-93.740
750	4.5328 (-7.6061) {-312.829}	2.0123 (-5.7228) {-313.871}	0.9227 (-3.8536) {-317.215}	0.6768 (-3.1231) {-312.150}	-100.873
1000	4.9978 (-7.8440)	2.5671 (-6.3264)	1.0003 (-4.0571)	0.8013 (-3.5557)	-99.942
Lor. Conc. (100 µg.ml-1)	**Ratio 40/60**				
0*	0.6293 (-2.7937) {-200.727}	0.4654 (-2.0935) {-199.726}	0.2580 (-0.6417) {-201.200}	0.1986 (+0.0179) {-199.977}	-62.640
100	0.9929 (-3.9052)	0.4982 (-2.2623)	0.3011 (-1.0311)	0.217 (-0.209)	-78.980

	{-251.819}	{-253.076}	{-252.957}	{-251.543}	
250	1.2333 (-4.4336) {-250.041}	0.6707 (-2.9993) {-250.648}	0.4670 (-2.1373) {-249.378}	0.3969 (-1.7558) {-246.616}	-78.983
500	1.9858 (-5.5946) {-178.078}	1.9897 (-5.6948) {-174.811}	0.7999 (-3.4936) {-179.127}	0.7440 (-3.3657) {-176.682}	-58.688
750	2.6720 (-6.3179) {-178.836}	1.5324 (-5.0475) {-180.075}	0.9874 (-1.5967) {-188.349}	0.8231 (-3.6245) {-178.859}	-59.633
1000	3.2296 (-6.7799) {-184.705}	2.6078 (-6.3654) {-183.011}	1.1113 (-4.0244) {-187.635}	0.880 (-3.7958) {-185.374}	-61.847

*SDS/CTAB mixed system

Table 4: The conductivity values of Lor.: SDS/CTAB % mixture at different fraction ratios and different temperatures in Lor. (100 µg.ml^{-1})

SDS/CTAB 2% Wt	L(µS.cm^{-1})			
	298.15K	303.15 K	308.15 K	313.15 K
0	1671	1554	1543	1538
10	1703	1680	1674	1666
20	1235	1223	1209	1050
30	1765	1847	1841	1777
40	2067	2307	2288	2202
50	3661	3009	3002	2896
60	3783	3211	3277	3011
70	3781	3280	3065	3008
80	3487	3472	3322	3313
90	3841	3862	3655	3788
100	4123	3872	3796	3667

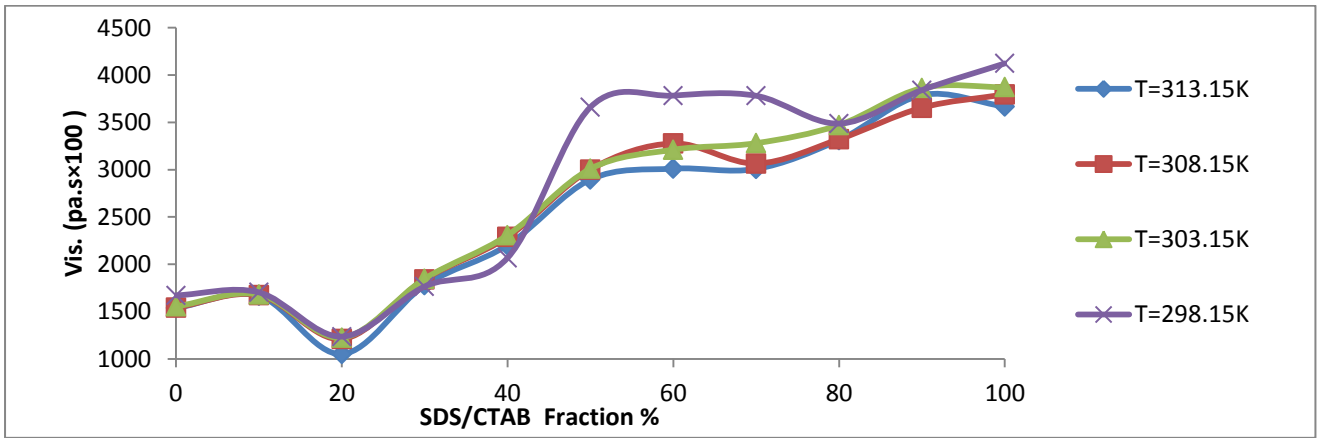

Figure 5: the relationship between conductivity and SDS/CTAB% fraction in Lor. (100 µg.ml^{-1}) at different temperature

Conclusions

The suggested method described simple, rapid and low coast method for determination of Loratadine in pharmaceutical preparation. The using of distilled water with methanol as solvent encourages the application of this method in routine quality control analysis of Loratadine in pharmaceutical forms. The Loratadine viscosity increase with surfactant and entropy decrease for micelles system.

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