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STUCTURAL AND SPECTROSCOPIC STUDY OF Cu(II) – TAURINE –HEXAMINE TERNARY COMPLEX: DETERMINATION OF THE STABILITY CONSTANTS IN METHANOL – WATER MIXTURES

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ABSTRACT: Stoichiometry and apparent stability constant (K_C) of the complex formed between Cu(II), hexamine and taurine were determined in water and methanol-water mixtures (% methanol w/w: 3.11; 6.15; 10.4; 15.2; 19.9 and 25.3) by UV–vis spectroscopy at 25^o C and constant ionic strength (0.05 M, sodium chloride). Stoichiometry of the ternary complex (1:1: 2, metal: hexamine: taurine) is not modified with an increase in methanol percentage in the analyzed interval. The value of K_C in water is greater than in the binary solutions. The effects of changing solvent composition on K_C data were explained by linear solvation free energy relationships using the solvatochromic parameter of Kamlet and Taft (α, ß and π*). Multiple linear regression analysis indicates that the hydrogen bond donating ability (α) of the solvent and non-specific interactions (π*) play an important role in the degree of occurrence of the reaction. The effect of temperature on K_C was also analyzed by assessing standard entropy and enthalpy variations of the reaction in water. Finally, the structure of the complex was investigated using IR spectroscopy, where the ligand exhibits small structural changes upon complexation.

INTRODUCTION: Taurine, α-aminoethane sulfonic acid, is a derivative of the sulfur-containing amino acid cysteine. It is one of the most abundant free amino acids in the human body and is widely distributed in biological fluids and tissues. [1] Taurine has many physiological functions as an antioxidant, neurotransmitter and toxinicide, and in conjugation of bile acids, modulation of the levels of intracellular ions (e.g. calcium, potassium, sodium), membrane stabilization, and osmosis. [2-3]

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Taurine plays an important role in prenatal development, especially in neural development as an inhibitory and neuroprotective neurotransmitter and neuromodulator.[4] Changes in taurine levels in physiological fluids and tissues occur in various diseases or pathological conditions such as psychosis, inflammation, hepatic damage, sepsis, and cancer.[5]

To date, several methods have been developed for the determination of taurine. These methods include gas chromatography,[6] high-performance liquid chromatography with amperometric detection,[7] HPLC with electrospray ionization/ mass spectrometry,[8-9] and capillary electrophoresis.[10-11] These methods differ in sensitivity, selectivity, specificity, and

susceptibility to interferences. HPLC with mass spectrometry has good sensitivity, selectivity and specificity. However, mass spectrometers are expensive and complicated, which limits the routine application of this technique in clinical research, particularly in studies calling for the analysis of many samples.

Several pre column derivatizing agents have been used for the determination of taurine; o-phthalaldehyde, 4-(5,6-dimethoxy-2- phthalimi dinyl)-2-methoxyphenylsulfonyl chloride [12] and fluorescamine [13]. The *o*-phthalaldehyde derivative is unstable, which affects the accuracy and reproducibility of taurine analysis. 4-(5,6-Dimethoxy- 2-phthalimidinyl)-2 -methoxy phenylsulfonyl chloride and fluorescamine derivatives can be used for the determination of taurine, but the pre-treatment procedures are difficult and time-consuming (>20min).

Literature review revealed few methods for the spectrophotometric determination of taurine, [14-15] using 2, 4-dinitro-1-fluorobenzene and (phenol / sodium hypochlorite) as reagents. Yet, these methods either applied tedious time consuming procedures or offered low sensitivity values.

The interaction of a metal ion with a ligand changes considerably with the polarity and ability to form hydrogen bonds of the reaction medium, but this effect has not been widely studied. Because of this, in this work we analyzed the interaction between Cu (II), hexamine, and taurine (TAU) in different methanol–water (CH_3OH– H_2O) solutions by means of UV–vis spectroscopy to show how the solvent affects the apparent stability constants (K_C) of the reaction.

Linear solvation free energy relationships utilizing the solvatochromic parameter of Kamlet and Taft allows the analysis of solute–solvent interactions and the calculation of the K_C value in CH_3OH–H_2O mixtures up to a methanol percentage of 25.3% w/w. Furthermore, we analyzed the effect of temperature on the reaction in water, evaluating the standard enthalpy and entropy variations of the reaction. In addition, the main structural features of the complex were obtained by Infrared Spectroscopy (IR).

Experimental:

Reagents:

Taurine (**Fig. 1**) was kindly provided by Kevok Pharmaceutical Company (Cairo, Egypt). Cupper chloride ($CuCl_2$), hexamine, sodium chloride (NaCl), boric acid and sodium hydroxide required for preparation of borate buffer, and spectroscopic grade CH_3OH from Merck were used without further purification. Water was delivered by a Milli-Q-water purification system.

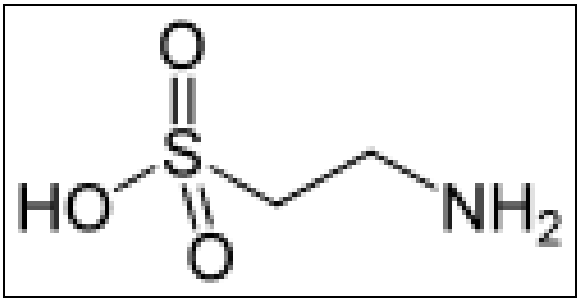


FIG. 1: STRUCTURAL FORMULA OF TAURINE

UV–VIS spectroscopic measurements:

The stoichiometric composition of the complex in water and in CH_3OH-H_2O mixtures (% CH_3OH w/w: 3.11; 6.15; 10.4; 15.2; 19.9 and 25.3) was determined by the molar relation method.[16] The concentration of TAU was kept constant (16 $x10^{-5}$ M) and the concentrations of $CuCl_2$ and hexamine varied between 16 $x10^{-6}$ M and 5 $x10^{-4}$ M (this is to say, a metal and hexamine/TAU ratio of 0.1–3.1). The ionic strength was kept constant (0.05 M) by addition of NaCl. The solutions were stabilized at 25.0 ± 0.1^{o}C until reaching equilibrium (1 h of reaction). Subsequently, the spectra were recorded in a Spectro. UV-Vis. double beam PC scanning spectrophotometer, UVD – 2950, Labomed inc.; 1 cm-optical path, in the 250–350 nm intervals. In the determination of K_C of the complex, in the different reaction media, a spectrophotometric method designed by Ferretti et al.[17] was used. This procedure requires the preparation of solutions of increasing concentration, maintaining the molar ratio of TAU to metal and hexamine in the stoichiometric proportion.

The analytic concentrations of TAU and $CuCl_2$/hexamine in the reaction mixture were from 3.2 $x10^{-5}$ to 3.8 $x10^{-4}$ M and from 16 $x10^{-6}$ to 19 $x10^{-5}$ M respectively. The ionic strength was fixed to 0.05 M with NaCl. After 1 h of reaction at 25.0 ±

0.1°C, the respective absorbance values were read at the maximum absorption wavelength of the complex. The effect of temperature on the K_C of the reaction in water was determined by means of the procedure described above. The temperature interval analyzed ranged from 25.0 to 45.0°C.

RESULTS AND DISCUSSION:

Complex stoichiometry in water and methanol-water solutions

Generally, amino acids develop their basic and acid function through the NH_2 and carboxylic groups, respectively. On the contrary, taurine contains an aminic and a SO_3^- group. However, its ligand properties depend on the presence of the aminic nitrogen atom so that it acts as a monodentate ligand. Although taurine is a simple compound, only few studies can be found in the literature on its behavior as a ligand towards cations.[18] This is probably due to the poor stability of its complexes. As a consequence, ternary complex formation could be an alternative providing much better stability constants.

Taurine is a weak UV absorbing drug. Through this work it was possible to carry out a simple ternary complex formation reaction between taurine, hexamine and Cu (II) through the addition of aliquot volumes of taurine standard stock solution to a 10 mL volumetric flask to cover the working concentration range of 2.0-20.0 µg/mL. One mL of borate buffer of pH 7 followed by 1 mL of 10% w/v hexamine were added, followed by 1 mL of $CuCl_2$ and 1 mL of 0.05 M NaCl. The volume was then completed to the mark with either water or methanol-water mixtures.

The UV spectra of the formed complex in water and in methanol-water mixture are very similar where the absorption spectrum is characterized by a single band at 279 nm. In the presence of methanol (25.3% w/w), the band present practically doesn't change. Figures 2 and 3 illustrate the evolution of the UV spectra in H_2O and CH_3OH – H_2O, respectively, for different [Cu (II), hexamine] / [TAU] molar ratios varying between 0 and 3.

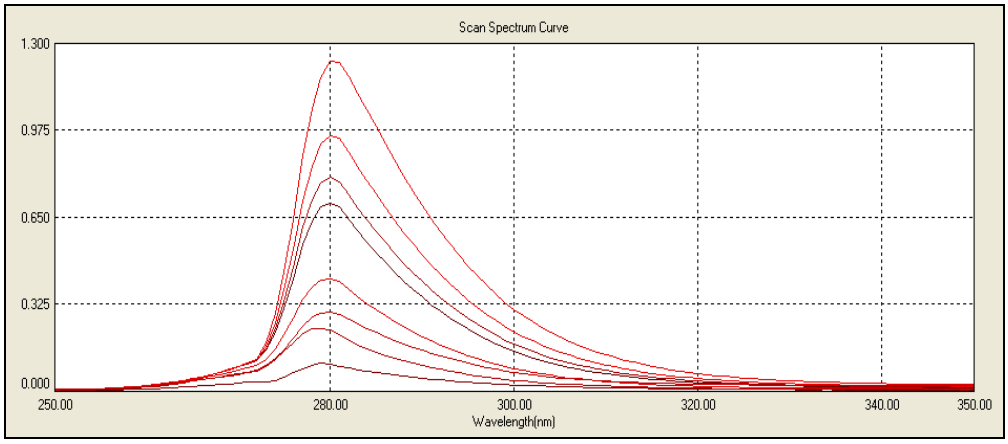


FIG.2: ABSORPTION SPECTRA OF TAURINE COMPLEXED WITH CULCL$_2$ FOR MOLAR RATIO 0–3 IN WATER AT 25°C

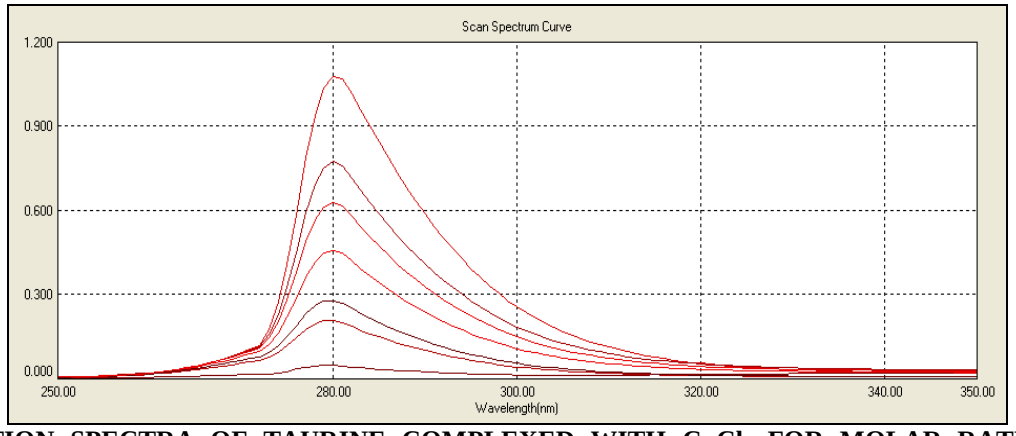


FIG.3: ABSORPTION SPECTRA OF TAURINE COMPLEXED WITH $CuCl_2$ FOR MOLAR RATIO 0–3 IN METHANOL WATER (25.3% w/w) AT 25°C.

By means of the molar ratio method, the complex stoichiometry was determined to be 1:1:2 (metal: hexamine: drug) in pure water and in the presence of increasing amounts of methanol (% CH_3OH w/w: 3.11; 6.15; 10.4; 15.2; 19.9 and 25.3). In all cases it was observed that the absorbance values *vs.* molar ratio [Cu (II), hexamine] / [TAU] plots at λ_{max} of the complex show an inflexion at the ratio 0.5. These results are shown in **Fig. 4, 5**.

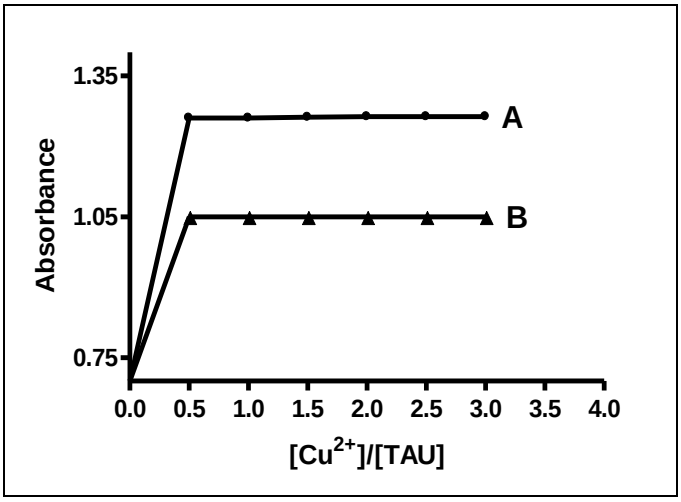


FIG. 4: ABSORBANCE *VS.* [$CuCl_2$]/[TAURINE] MOLAR RATIO PLOTS AT λ_{max} 279 nm iN WATER (A), IN METHANOL- WATER (25.3% w/w) (B) AT 25^{O}C.

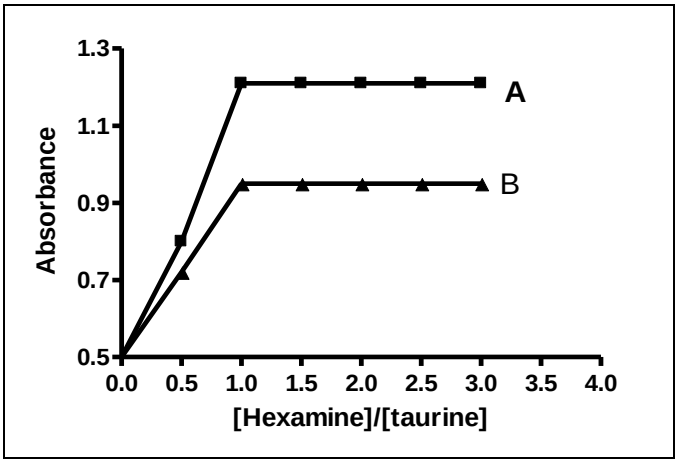


FIG.5: ABSORBANCE *VS.* [HEXAMINE]/[TAURINE] MOLAR RATIO PLOTS AT λ_{max} 279 nm IN WATER (A), IN METHANOL- WATER (25.3% w/w) (B) AT 25^{O}C

Determination of the apparent constant of stability in water–methanol solutions:

The K_C of the ternary complex was determined using the procedure describe above. Considering now that the stoichiometry of the complex is 1:1: 2, the reaction can be represented in a simple form as:

$$M + 2L \rightleftharpoons C \qquad (1)$$

Where M: $CuCl_2$, L: ligand TAU, C: metal complex. Since C absorb radiation at the selected wavelength and that, at the same wavelength, the metal ion does not absorb radiation, the final expression that permits to determine K_C is[17]

$$\frac{A_e}{[M_o]^{1/3}} = \frac{2\,\varepsilon_L - \varepsilon_C}{(4K_C)^{1/3}} + \varepsilon_C\,[M_o]^{2/3} \qquad (2)$$

Where A_e is the absorbance of the reaction mixture in equilibrium, $[M_o]$ is the initial molar concentration of metal, ε_L and ε_C are the molar absorptivity of the ligand and complex, respectively. Eq. (2) allows the determination of the K_C values under different reaction conditions. It may be noticed that the calculation of K_C requires knowing ε_L and ε_C. The ε_L value was previously determined, whereas ε_C is obtained from the slope of the straight line in Eq. (2).

Experimental data (A_e) at 279 nm (λ_{max} complex) in H_2O and in the CH_3OH – H_2O mixtures were represented graphically following Eq. (2) (**Fig. 6**). As expected, if this equation is satisfied, a straight line of negative intercept is obtained at λ_{max} complex.

The expressions, ε_C and K_C values obtained were:
In pure water:

$$\frac{A_e}{M_o^{1/3}} = -0.107 + 6329\,M_o^{2/3}$$

$R^2 = 0.9993$, $\varepsilon_C = 6329$ L. mol^{-1}. Cm^{-1}, $K_C = 5.17 \times 10^{13}$

In CH_3OH – H_2O (25.3% w/w):

$$\frac{A_e}{M_o^{1/3}} = -0.394 + 5453\,M_o^{2/3}$$

$R^2 = 0.9993$, $\varepsilon_C = 5453$ L. mol^{-1}. Cm^{-1}, $K_C = 6.63 \times 10^{11}$

TABLE 1: APPARENT STABILITY CONSTANTS VALUES OF THE COMPLEX (LOG K_C) AND SOLVATOCHROMIC PARAMETERS IN WATER AND METHANOL-WATER MIXTURES AT 25^{O}C AND IONIC STRENGTH 0.05 M DETERMINED WITH EQ. (2).

%CH_3OH (w/w)	Log K_C	α	β	π*	D
0	13.90	1.17	0.47	1.09	85
3.11	13.60	1.16	0.475	1.07	83.3
6.15	13.53	1.155	0.479	1.06	81.6
10.4	13.00	1.14	0.486	1.04	79.3
15.2	12.70	1.13	0.493	1.02	76.64
19.9	12.62	1.12	0.499	0.992	74.06
25.3	11.80	1.11	0.508	0.953	71.09

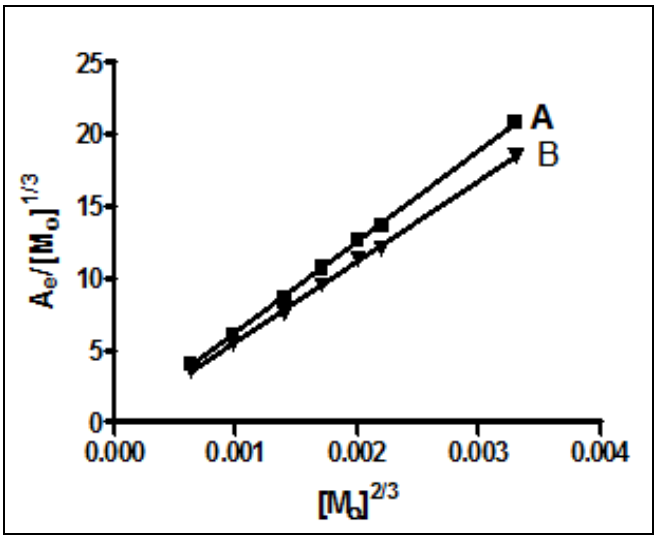


FIG. 6: DETERMINATION OF APPARENT STABILITY CONSTANTS OF THE COMPLEX AT 279 nm IN WATER (A), IN METHANOL- WATER (25.3% w/w) (B) ACCORDING TO EQ. (2)

The very good correlation coefficients and K_C values obtained satisfy Eq. (2), and thus confirm the stoichiometry established previously by the molar relation method. **Table 1** presents the K_C values obtained, in the CH_3OH-H_2O mixtures used for the analysis of the reaction at 25° C and 0.05 M ionic strength. The complex stoichiometry does not change, but the value of K_C in water (5.17×10^{13}) is greater than in CH_3OH-H_2O 25.3% w/w (6.63×10^{11}), indicating that Cu(II) is more readily complexated in pure water than in the presence of methanol.

Effects of solvent and temperature on the apparent stability constants:

Solvents play an important role in physical and chemical processes. Specifically, the chemical equilibria are modified due to changes in free energy solvation of the participating species. This effect is closely related to the nature and extent of solute–solvent interactions (non-specific and specific), developed locally in the immediate vicinity of the solutes.[17] **Table 1** summarizes the dielectric constants (D) values and the solvatochromic parameters (α, β and π) of CH_3OH-H_2O mixtures, as well as the log K_C. The parameter α represents the hydrogen bond donation (HBD) ability of the solvent, β is its hydrogen bond acceptance (HBA) or electron pair donation ability to form a coordinative bond, and π^* is its polarity/polarizability parameter. The values for these parameters for the ternary mixture used were calculated using the following equation[20]

$$P_{Mixture} = P_{H2O}X_{H2O} + P_{CH3OH}X_{CH3OH} \quad \textbf{(3)}$$

Where P is the property of interest (D, α, β or π) and X is the molar fraction of the components. The values of D, α, β and π^* corresponding to pure solvents (H_2O and CH_3OH) have been taken from the literature.[21] It may be noted that the log K_C decreases as the CH_3OH % increases in the reaction medium (0–25.3% w/w). **Fig. 7** shows the variation in log K_C in relation to the (α) parameter and a linear variation (log K_C = 31.99α -23.5 (R^2 = 0.995)) can be observed up to 15.2% of CH_3OH-H_2O (a mixture of 1.02). Similar variations are observed when considering the dependence of log K_C with the other parameters mentioned. In other words, a simple solvent property does not interpret by itself changes in K_C in the whole interval of compositions studied.

As a result, to analyze the solvent effects on the K_C quantitatively we used the multi parameter equation of Kamlet–Taft, also known as linear solvation energy relationship,

$$\text{Log } K_C = A_o + a\alpha + b\beta + P\pi^* \quad \textbf{(4)}$$

Where A_0, a, b and p are coefficients characteristic of the process and indicative of its sensitivity to the accompanying solvent properties, α, β and π^* hold the previously indicated meaning. The following regression equation was obtained using the software Xlstat.[22] Standard deviations are indicated in parenthesis,

$$\text{Log } K_C = 318\ (66.3) + 528\ (94.5)\ \alpha + 187\ (34.6)\ \pi^* + 3.4\ (0.663)\beta \quad \textbf{(5)}$$

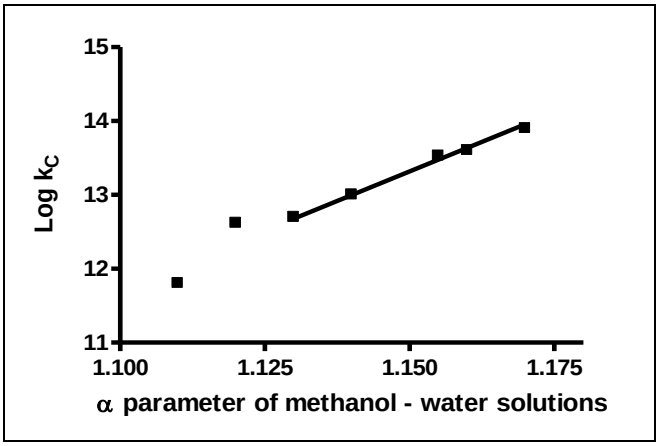


FIG.7: VARIATION OF THE LOG K_C OF THE COMPLEX WITH THE α-PARAMETER OF METHANOL–WATER SOLUTIONS (0–25.3% w/w).

This equation has high statistical quality and the variables selected explain 99.2% of the variability of log K_C. The relative contributions of the parameters are: α 72.8%, π* 26.7% and β 0.51%. This suggests that the HBD of the solvent is the most important factor, that the polarity/polarizability parameter plays a relatively smaller role, and finally that the β term has very little significance on the apparent stability constants of the complex in CH_3OH-H_2O mixtures. The positive value of α indicates that log K_C increases as the HBD capacity of the solvent increases, whereas the positive sign of π* shows that K_C increases as the solvents ability to stabilize a charge or a dipole by its own dielectric effect increases. These effects may be interpreted considering that the analyzed reaction takes place in more than one step, influenced by the solvent in a different manner.

The complexation reaction is preceded by the ligand ionization. The presence of water in the reaction medium appears to favor this step as well as the solvation of the ligand anion. The solvation of anions is effective in protic solvents in which a hydrogen bond may be formed between the proton of the solvent and lone pairs of the anion.[19] Moreover, cupper chloride has a high affinity for water and exists as the octahedral hexahydrate ($(H_2O)_6^{+2}$), which is stabilized through hydrogen bonding. In this solvation step, specific interactions (α parameter) contribute significantly.

As may be expected, if the reacting ions (ligand anion and metallic cation) are more solvated, free energy decreases and reactivity will be lower in CH_3OH-H_2O than in pure H_2O. On the other hand, when the complex is formed (Cu (II) – hexamine-TAU_2^+) non-specific interactions (parameter π*) stabilize the complex formed and favor or shift the equilibrium toward its formation. A good lineal correlation is observed when the predicted values of log K_C using Eq. (5) are represented graphically against the experimental values. **Table 2** summarizes these values and their confidence interval, calculated with a significance level of 0.05. The effect of temperature on K_C was analyzed in the interval from 25.0 to 45.0°C, being H_2O the reaction medium. The thermodynamic parameters of this reaction were determined using the classic van't Hoff equation.[23] Standard enthalpy (ΔH^o) and entropy (ΔS^o) variation were obtained in the usual manner from the slope and intercept of the lineal plot of log K_C vs. 1/T (**Fig. 8**). This reaction in H_2O is exothermic (79.2 Kj/mol) with a negative ΔS^o value (52.7 J/K mol), the latter being characteristic in complexation reactions such as the one analyzed in this study.

TABLE 2: EXPERIMENTAL AND CALCULATED (EQ. 5) APPARENT STABILITY CONSTANT (K_C) VALUES AND THEIR CONFIDENCE RANGE WITH A SIGNIFICANCE LEVEL OF 0.05

Log K_C (experimental)	Log K_C (calculated)	Lower value (95% confidence range)	Upper value (95% confidence range)
13.90	13.92	13.69	14.11
13.60	13.58	13.41	13.79
13.53	13.58	13.33	13.73
13.00	13.04	12.81	13.19
12.70	12.65	12.52	12.88
12.62	12.61	12.44	12.81
11.80	11.84	11.63	11.97

Linearity and range:

Under the described experimental conditions, a linear relationship was established by plotting absorbance readings for the studied ternary complex against drug concentrations in µg/mL. The concentration range was found to be 2.0-20.0 µg/mL. The high value of the correlation coefficients (r-value > 0.999); with small value of intercept indicate the good linearity of the calibration graph over the working concentration range. Statistical analysis of the data gave small values of the standard deviation of the residuals ($S_{y/x}$), of slope (S_b) and of intercept (S_a) (Table 3).[24] Thus, indicating low scattering of the points around the calibration curve.

Limit of quantitation and limit of detection:

Detection limit (LOD) is the lowest concentration of the drug that can be detected, but not necessarily quantitated, under the stated experimental conditions. The limit of detection is generally quoted as the concentration yielding a signal-to-

noise ratio of 3:1[25] and is confirmed by analyzing a number of samples near this value using the following equation:

The signal-to-noise ratio s = H/h

Where H = height of the spectrum corresponding to the drug

h = absolute value of the largest noise fluctuation from the baseline of the spectrum of a blank solution.

While the limit of quantification (LOQ); is the lowest concentration of the analyte that can be determined with acceptable precision and accuracy. It is quoted as the concentration yielding a signal-to-noise ratio of 10: 1 and is confirmed by analyzing a number of samples near this value.[25] The calculated values are listed in **Table 3**.

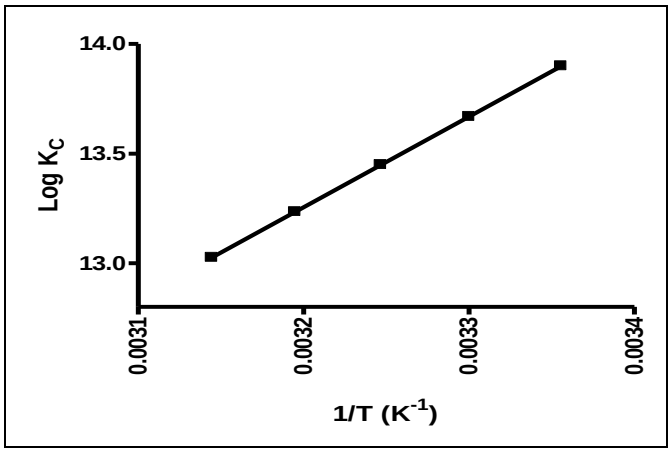


FIG. 8: PLOT OF LOG K_C AGAINST 1/T ACCORDING TO VAN'T HOFF EQUATION FOR THE COMPLEXATION REACTION STUDIED IN WATER.

Method Validation:

TABLE 3: PERFORMANCE DATA OF THE PROPOSED METHOD

Parameter	Proposed method
Concentration range (µg/mL)	2.0-20.0
LOD(µg/mL)	1.5
LOQ(µg/mL)	1.9
Correlation coefficient (r)	0.9997
Slope	0.01
Intercept	-0.13
Sy/x, S.D. of residuals	8.7x10-2
Sa ,S.D. of intercept	7.6x10-3
Sb ,S.D. of slope	6.9x10-3

Accuracy: The accuracy of an analytical method is defined as the similarity of the results obtained by this method to the true values. To test the validity of the method it was applied to the determination of pure samples of the concerned drugs over the working concentration ranges. The high percentages recoveries and small values of S.D. indicate the accuracy of the proposed method.

The accuracy of the proposed method was also evaluated by studying the accuracy as percent relative error (% Error) and precision as percent relative standard deviation (% RSD), and the results are shown in **Table 4**. The results obtained were compared with those obtained using the comparison method.[15]

TABLE 4: APPLICATION OF PROPOSED METHOD FOR DETERMINATION OF TAU IN ITS PURE FORM

Parameter	Taken (µg/mL)	Found (µg/mL)	%Found	Comparison method [15], %Found
	2.0	1.99	99.34	100.34
	5.0	4.99	99.87	100.87
	8.0	7.99	99.93	100.59
	10.0	10.02	100.23	
	15.0	15.08	100.53	
	17.0	17.13	100.77	
	20.0	20.08	100.38	
$\bar{X}$ ±SD			100.15±0.48	100.6±0.27
t test			0.11(1.94)	
F test			3.16(5.14)	
%RSD			0.48	
%Error			0.18	

*Figures between parenthesis are tabulated t and F values at P=0.05 [24]

Precision:

The intra-day precision was evaluated through replicate analysis of three different concentrations of the drug in pure form on three successive times. The inter-day precision was also evaluated through replicate analysis of three concentrations for a period of 3 successive days. The results of intraday and inter day precision are summarized in **Table 5**. The small values of RSD and % Error indicate high accuracy and precision of the proposed method, respectively.

TABLE 5: PRECISION DATA FOR THE DETERMINATION OF THE STUDIED DRUG IN PURE FORM BY THE PROPOSED METHOD

Taurine pure form	(2.0 µg/ml)	(10.0 µg/ml)	(20.0 µg/ml)
Intra-day precision,	100.45	100.67	100.89
%found	100.31	99.44	100.65
	99.95	99.83	100.49
$\bar{X}$±SD	100.24±0.26	99.98±0.63	100.68±0.21
%RSD	0.26	0.63	0.21
%Error	0.15	0.36	0.12
Inter-day precision,	99.78	100.53	100.59
%found	100.76	99.13	100.11
	100.13	99.87	99.31
$\bar{X}$±SD	100.22±0.49	99.84±0.71	100.02±0.65
%RSD	0.49	0.71	0.65
%Error	0.28	0.41	0.38

Complex separation and structure:

The formed complex was successively isolated and purified by preparative TLC using methylene-chloride: methanol (20:80, *v/v*). The solvent was removed by evaporation under reduced pressure, and the purity of the complex was tested by TLC. The TLC was performed using chloroform: methanol (30:70, *v/v*) as a developing solvent, where the R_f of taurine and ternary complex were 0.75 and 0.46 respectively, which in turn confirms the completeness of the complex formation reaction. After confirmation of the purity of the complex; infra red spectroscopy was performed to elucidate the structure of the resultant product.

The IR spectrum of the studied complex showed a slight shift in the bands of the main functional groups in taurine; such as the shift in the stretching band of the sulphonic acid S=O from 1200 cm^{-1} in TAU to 1280 cm^{-1} in the complex, bending vibration band of N-H of primary amine from 1600 cm^{-1} in TAU to 1500 cm^{-1} in complex (**Figs. 9a-9b**). This means that the aforementioned functional groups were not altered through the complexation reaction. On the other hand, new bands appear in the complex; a band at 2800 cm^{-1} corresponding to stretching vibration of alkyl groups, and another band at 3400 cm^{-1} corresponding to stretching vibration of O-H which appeared due to the incorporation of water in the complex structure. Such finding, in addition to previous reports [26-27]suggests the complex structure mentioned in **Scheme 1**.

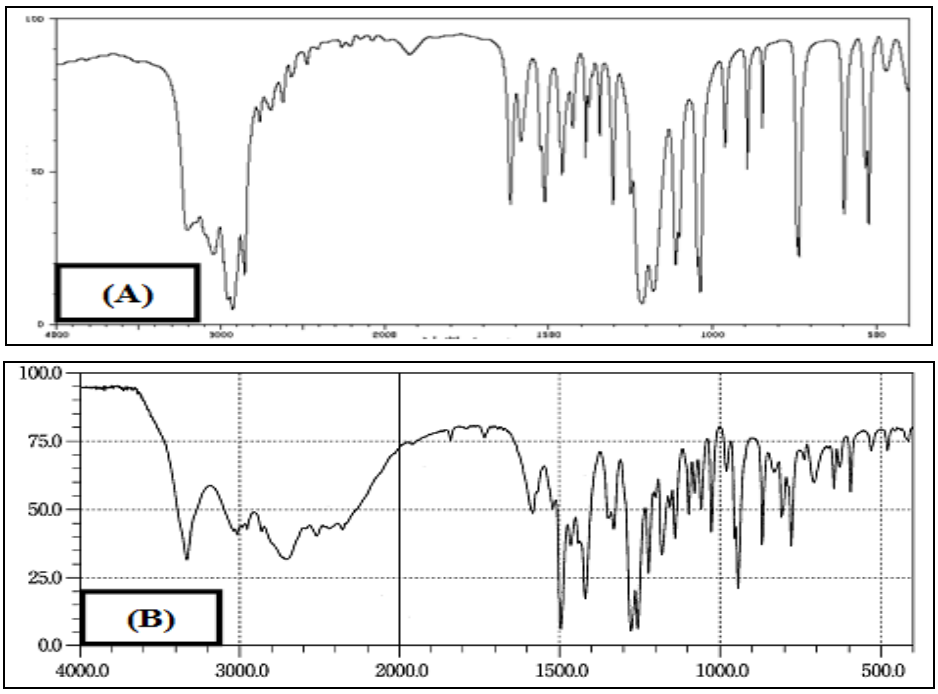
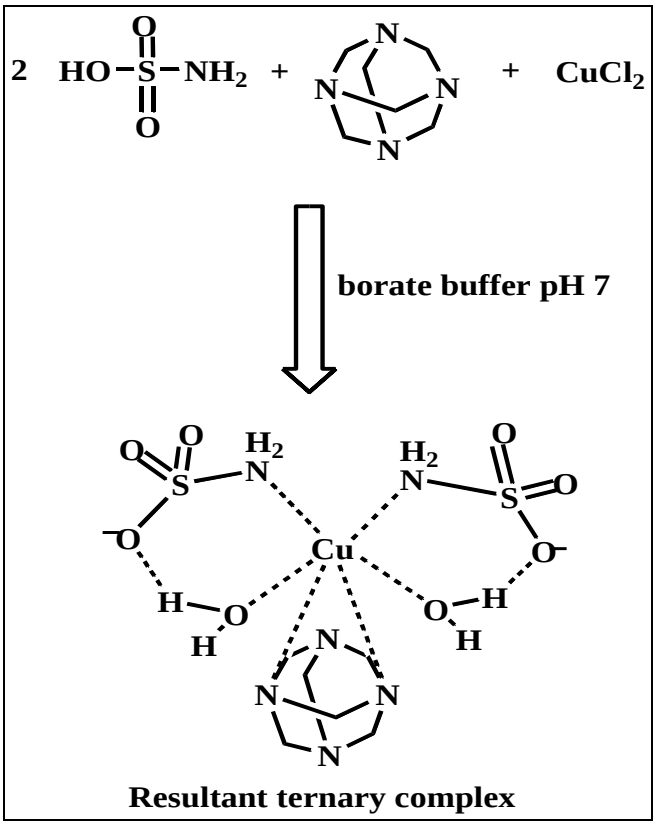


FIG. 9: IR SPECTRUM OF TAURINE (A), AND TERNARY COMPLEX (B)



SCHEME 1: PROPOSAL OF THE REACTION MECHANISM

CONCLUSION: A simple, sensitive and rapid method has been developed for determination of the stoichiometry and apparent stability constant (K_C) of taurine ternary complex in water and methanol-water mixtures. The value of K_C in water was found to be greater than in the binary solutions. The effects of changing solvent composition on K_C data were subjected to detailed investigation. The effect of temperature on K_C was also analyzed by assessing standard entropy and enthalpy variations of the reaction in water. Furthermore, the structure of the complex was investigated using IR spectroscopy.

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