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Original Article

# The Formation Analysis of Ca (II), Mg (II), Zn (II) and 5-Hydroxysalicylic Acid Binary Complexes in Cetyltrimethylammonium Bromide Cationic Micelles

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## ABSTRACT

**Aim:** The aim of the present study is to confirm the species formed under the used experimental conditions and to validate the models by statistical treatment of the data. As the results obtained in this study have specific applications in extraction metallurgy, nuclear energy industry, and analytical methods, medical, environmental, and industrial research. These applications all require stability constant values of high reliability and sources of critically evaluated published constants are referenced. Stability constant is useful physical entity, which explains the importance and function of various complexes in biological systems. **Background:** Despite the availability of information about the effect of organic-water media, anionic-surfactants media on the stability of binary complexes, this data related to 5-Hydroxysalicylic acid with essential metals Ca (II), Mg (II), Zn (II) in cationic-surfactant medium is carried out in this study. **Materials and Methods:** Aqueous solutions of Ca, Mg Zn and Cetyltrimethylammonium Bromide were prepared using triple-distilled water. The alkali metric titrations were carried out in a medium containing varying compositions of Cetyltrimethylammonium Bromide (CTAB)-water mixtures (0.0-2.5% w/v) used by maintaining an ionic strength of 0.16 mol $dm^{-3}$ with sodium hydroxide at 303.0+0.1 K. An ELICO (Model L1-120) pH-meter (readability 0.01 pH units) pH meter was used to carry out the pH values. A well-defined computer algorithm known as MINIQUAD75 was used to perform an analysis on the complex species models. On a few different complex species, exhaustive modelling work has been done. Results: The formed metal-ligand complexes in between Ca(II), Mg(II), Zn(II) and Cetyltrimethylammonium bromide are $ML_2H_3$, $ML_2H_4$, and $ML_3H_4$. These complexes have been identified to be the predominant complex species that have formed. On the basis of the statistical parameters, the chemical modelling approach that provides the best fit has been adopted. The complex species were verified through the statistical study of the data. Based on electrostatics, the change in stability of complex species as a function of surfactant composition has been shown, the distribution of chemical species with respect to pH and compositional diversity is also shown explores how possible complicated equilibria. The data acquisition of acid-base equilibria and determination of stability constants were performed using MINIQUAD75 algorithm and the distribution patterns of the complexes with varying pH and compositions of surfactants were presented from the plots of SIM run data. **Conclusion:** A study of the chemical speciation of ternary complexes of Ca(II), Mg(II), and Zn(II) with 5-HSA in micellar medium reveals the compartmentalization of metabolic reactions. The study gives an insight into the metal availability /metal transport in bio fluids. The binary complexes make the "metal available" in biological systems due to their decreased stability. It is observed that the stability constants are more affected by concentration of alkali than other parameters like concentration of acid, ligand and others.

**Keywords:** Binary complexes, Chemical speciation, Cetyltrimethylammoniumbromide, Stability constants, Anionic surfactant, Cationic micelles, Complexes.

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## INTRODUCTION

Cetyltrimethylammonium Bromide (CTAB) is a very good anionic surfactant; it possesses noticeable influence on the bulk physiological system properties. They are able to dissolve, concentrate and compartmentalize ions and molecules.[1] Aqueous micellar media has wide applications in pharmaceutical industries, analytical chemistry, chemical synthesis, and in industrial processes. Energy storage is one of the important areas where micelles are used.[2,3] Amphiphilic molecules with hydrophobic and hydrophilic parts combine to form micelles in water at a certain concentration.[4] Micellar systems have the ability to change the acid-base balance. This chemical equilibrium shift can be explained by differences in the properties of the bulk solvent and the interfacial region, as well as perturbations of the acid-base balance due to the electrostatic field effect of the charged interface.[5] Potentiometric analysis was performed in cationic and

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anionic micelles to identify the dissociation equilibria.[6] Their *pKa* values have been found to change to approximately 0.5-3.0 in anionic micelles. An investigation on the chemical equilibria of different phenols, amines and carboxylic acids have been done in aqueous micellar solutions.[7] In the previous investigation done by different authors reported chemical equilibria using compounds containing phenols, carboxylic acids and amines in micellar media.[8]

Chemical speciation is an important study which is used in human biology,[9] nutrition, toxicology,[10] and clinical practice to determine the quantities of different forms of an element in a sample. Speciation affects an element's toxicity and bioavailability.[11-13] The speciation analysis of harmful and necessary metal ion complexes helps clarify the role of biological active site cavities and drug residue interacting with the metal ion. Number of studies has been performed on chemical speciation in aqueous media under the same conditions as in natural systems. These are used as models for the systems that exist in natural water and bio fluids. Nevertheless, Biosystems are linked to low dielectric mediums of varying magnitudes, and metabolic reactions are carried out in rigid compartments. Many other media have been used to investigate the complexation equilibrium; among these are dimethylformamide-aqueous mixture,[14] dioxane-water,[15] ethylene glycol-water,[16] 1, 4 dioxan-water,[17] propanediol-water[18] and DMSO-water.[19] Taking all of the aforementioned into account, work on binary complexes of Ca (II), Mg (II), and Zn (II) with 5-hydroxysalicylic acid complexes is required, as most complexes of calcium, magnesium, and zinc show tremendous metabolic activity.

## MATERIALS AND METHODS

### Materials

The materials required to perform this investigation is 0.05 M of 5-hydroxysalicylic acid (5-HSA) solution (TCI, India), which is prepared by dissolving the substance in a deionized water. To make 5-hydroxysalicylic acid better soluble, acidic medium is used, where Hydrochloric acid was employed an acidic solution, it also keeps the acid concentration of the ligand at 0.05 M. cationic micelles were prepared from cetyltrimethylammonium bromide (Merck, India). Sodium chloride (Qualigens, India) is used to the ionic strength of the system under this study, to maintain the ionic strength of a system. Calcium, magnesium and zinc (E-Merck, Germany) metal ions solution were prepared by taking their respective salt solutions as raw materials using deionized water and some amount 0.05 M HCl in order to prevent hydrolysis and to increase the solubility. All the metal ion solutions were standardized using standard EDTA solution. To determine errors in solution concentration, the data were analyzed using a one-way classification.[20] The Gran Plot method[21,22] is used to calculate the concentrations of acid and base.

### Instrumentation

A pH meter (ELICO, LI-120) was used to carry out a potentiometric titration. The instrument was calibrated at acidic and basic pH using 0.01 M borax and 0.05 M potassium

**Table 1: Initial component concentrations (in mmol) in CTAB-water formulations for metal ligand titrations.**

| % w/v CTAB | TM0 | | | TL0(5-HSA) | TL0:TM0 |
|---|---|---|---|---|---|
| | $Ca^{II}$ | $Mg^{II}$ | $Zn^{II}$ | | |
| 0.0 | 0.1024 | 0.1032 | 0.1040 | 0.2478<br>0.3755<br>0.4988 | 2.50<br>3.75<br>5.00 |
| 0.5 | 0.1024 | 0.1032 | 0.1040 | 0.2483<br>0.3742<br>0.4958 | 2.50<br>3.75<br>5.00 |
| 1.0 | 0.1024 | 0.1032 | 0.1040 | 0.2493<br>0.3744<br>0.4988 | 2.50<br>3.75<br>5.00 |
| 1.5 | 0.1024 | 0.1032 | 0.1040 | 0.2490<br>0.3781<br>0.4978 | 2.50<br>3.75<br>5.00 |
| 2.0 | 0.1024 | 0.1032 | 0.1040 | 0.2480<br>0.3764<br>0.4991 | 2.50<br>3.75<br>5.00 |
| 2.5 | 0.1024 | 0.1032 | 0.1040 | 0.2489<br>0.3782<br>0.4977 | 2.50<br>3.75<br>5.00 |

hydrogen phthalate solutions. The titrations were performed at 303.0 K using NaCl as to maintain the ionic strength of 0.16 mol.dm$^{-3}$, cetyltrimethylammonium bromide compositions were used having the concentrations ranging from 0.0 to 2.5% w/v. To account for variations and errors caused by using a glass electrode, a correction factor is used.[23,24]

### Analytical Techniques

Titrations with a strong acid-base solution were regularly performed prior to experimental titrations to ensure that the electrodes were adequately equilibrated with the solvent. All the titrations carried out using a volume of 50 mL titrand along with 1 mmol mineral acid. Titrations of 1:2.5, 1:3.75 and 1:5.0 metals to ligand ratios were performed using 0.4M NaOH. Table 1 contains the analytical concentrations of the components. Further details of the tests have already been announced.[25,26]

### Modeling Approach

SCPHD is one of the best computer program employed in this present study to calculate the correction factor[27] he stability constants of different metal ligand complexes are determined by using a computer program called MINIQUAD75,[28] where it uses the data obtained in acid-base titrations. The initial refinement and conjunction of Marquardt algorithm approached through limited least squares using MINIQUAD75 software program. It is necessary to use the correction factor and the protonation constants[29] of 5-HSA in order to calculate the stability constants of binary metal-ligand complexes. Based on electrostatic interactions and interactions of a solute with a solvent, we studied how the composition of a cationic surfactant affects the stability of complex species.

## RESULTS

Table 2 displays the results of the computer modelling study. The parameters such as lower $U_{corr}$ (deviations in component concentrations), lower, small and mean standard deviation, and mean validate the data through residual analysis.

### Analysis of Residuals

The present study accepts the models because the $\chi^2$ values are smaller than the table values. Kurtosis values indicate that the residuals in this study are leptokurtic in shape. The skewness values for Ca(II) range from -0.32 to 0.04, for Mg(II) from -0.53 to 1.02, and for Zn(II) from -0.03 to 0.15. These statistics show that the residuals are normally distributed. Thus, the data provided can be analyzed using the least squares method. In addition, crystallographic *R* values demonstrate the sufficiency of the model. As a result of these statistical properties, the best fitting models accurately represent the metal-ligand species in the CTAB medium.

## DISCUSSION

### Errors Impact on the Currently Accepted Modell

To verify that the final approved model is accurate, we introduced errors into the affected components as shown in Table 3. Due to the errors introduced in the affected components, certain complicated species were rejected and the standard deviation of the stability constants was increased. This means that the model is complete and acceptable. The inaccuracies have changed the

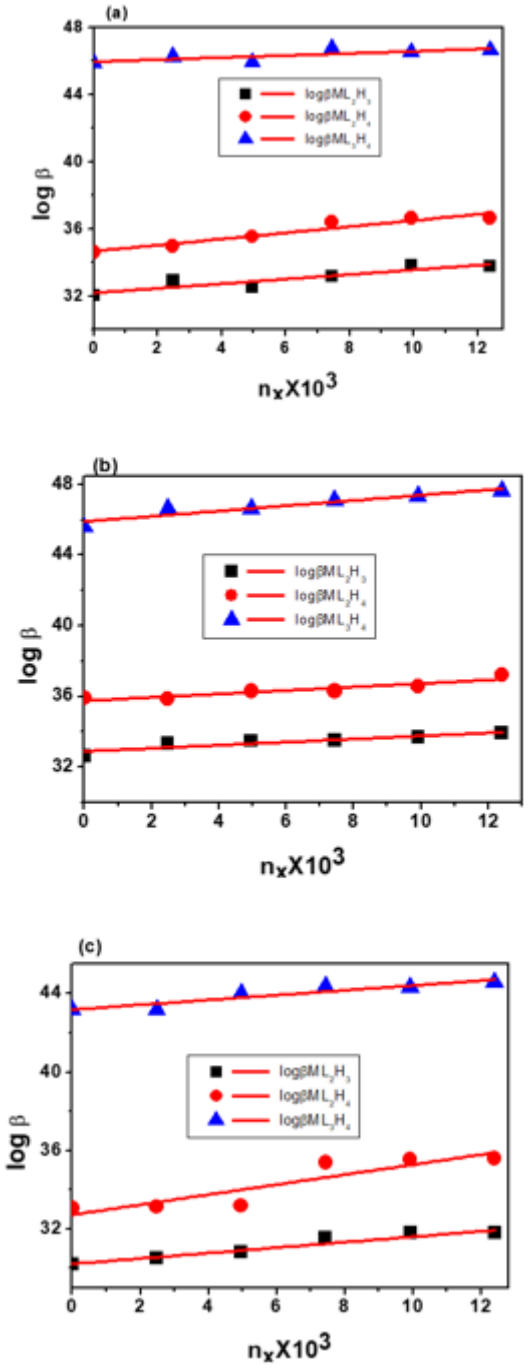


**Figure 1:** Changes in the total stability constant values of metal-5-Hydroxysalicylic acids complexes with mole fraction ($n_x \times 10^3$) of combinations of CTAB and water (a) $Ca^{II}$, (b) $Mg^{II}$ and (c) $Zn^{II}$, (■) log $\beta ML_2H_3$, (●) log $\beta ML_2H_4$, (▲) log $ML_3H_4$.

**Table 2:** $Ca^{II}$, $Mg^{II}$, and $Zn^{II}$-5-hydroxysalicylic acid complexes in CTAB-water mixtures: best-fit chemical model parameters.

| % w/v CTAB | log $\beta_{mlh}$ (SD) | | | pH-Range | NP | $U_{corr} \times 10^8$ | $\chi^2$ | Skewness | Kurtosis | *R*-factor |
|---|---|---|---|---|---|---|---|---|---|---|
| | $ML_2H_3$ | $ML_2H_4$ | $ML_3H_4$ | | | | | | | |
| $Ca^{II}$ | | | | | | | | | | |
| 0.0 | 32.06(22) | 34.64(50) | 45.89(62) | 2.3-9.3 | 32 | 15.51 | 8.23 | -0.02 | 2.10 | 0.0258 |
| 0.5 | 32.92(16) | 34.99(15) | 46.26(14) | 2.1-9.3 | 33 | 1.32 | 5.81 | -0.04 | 3.11 | 0.0068 |
| 1.0 | 32.53(39) | 35.55(27) | 45.95(25) | 2.3-9.0 | 26 | 5.21 | 13.49 | 0.04 | 10.19 | 0.0148 |
| 1.5 | 33.17(55) | 36.39(41) | 46.78(40) | 2.3-9.3 | 39 | 6.94 | 34.45 | -0.32 | 4.40 | 0.1682 |
| 2.0 | 33.83(45) | 36.64(40) | 46.52(48) | 2.3-9.2 | 40 | 9.72 | 7.73 | -0.28 | 3.49 | 0.1950 |
| 2.5 | 33.78(52) | 36.67(44) | 46.65(48) | 2.3-9.2 | 43 | 12.5 | 22.13 | -0.22 | 3.76 | 0.0221 |
| $Mg^{II}$ | | | | | | | | | | |
| 0.0 | 32.63(66) | 35.93(47) | 45.60(49) | 2.3-9.2 | 42 | 12.82 | 17.49 | -0.53 | 5.41 | 0.0228 |
| 0.5 | 33.36(25) | 35.87(23) | 46.62(42) | 2.3-10.5 | 61 | 53.45 | 36.58 | 1.02 | 12.49 | 0.0537 |
| 1.0 | 33.48(47) | 36.29(38) | 46.66(39) | 2.3-9.2 | 41 | 9.74 | 13.00 | -0.45 | 4.22 | 0.0201 |
| 1.5 | 33.51(63) | 36.30(30) | 47.10(26) | 2.3-9.69 | 43 | 17.50 | 19.78 | -0.12 | 2.19 | 0.0288 |
| 2.0 | 33.70(65) | 36.57(23) | 47.37(17) | 2.3-10.3 | 50 | 18.51 | 9.36 | -0.23 | 2.58 | 0.0310 |
| 2.5 | 33.93(48) | 37.22(47) | 47.66(20) | 2.7-10.4 | 24 | 21.43 | 3.56 | -0.52 | 3.09 | 0.0364 |
| $Zn^{II}$ | | | | | | | | | | |
| 0.0 | 30.18(30) | 33.04(52) | 43.19(58) | 2.2-9.1 | 57 | 33.33 | 104.42 | -0.03 | 9.02 | 0.0365 |
| 0.5 | 30.52(43) | 33.12(57) | 43.18(51) | 2.3-9.3 | 54 | 50.98 | 115.43 | 0.14 | 8.09 | 0.0496 |
| 1.0 | 30.81(69) | 33.18(39) | 44.05(39) | 2.2-9.3 | 49 | 19.57 | 23.18 | 0.02 | 6.50 | 0.0303 |
| 1.5 | 31.56(74) | 35.38(39) | 44.41(25) | 2.5-9.3 | 45 | 26.19 | 67.84 | 0.08 | 5.68 | 0.0374 |
| 2.0 | 31.81(29) | 35.54(30) | 44.31(42) | 2.3-9.3 | 53 | 36.00 | 25.60 | 0.01 | 3.77 | 0.0385 |
| 2.5 | 31.82(71) | 35.59(50) | 44.58(25) | 2.3-9.3 | 35 | 21.88 | 18.05 | 0.15 | 4.84 | 0.0351 |

order of the components: alkali component > acid component > ligand component > metal component > total volume component > log F component.

## The Effect of the Solvent

The dielectric constant is the most significant of each solvent's distinguishing characteristics. The stability of complexes that involve proton-ligand or metal-ligand is affected by factors such as the polarity of the solvent, as well as the impact that the solvent has on the metal ligand complex and the charges that the complexes carry. Several parameters, such as the dielectric qualities of the solvent, the ionic radius of the ions, and the electrostatic forces between the ions in solution, influence the relative acid and base strength characteristics. There is a net increase in ionization when an acid is ionized, which causes the solvent dielectric constant to drop. Additionally, this polarity shift can result in a rise in the weak acid protonation constant.

The effect of micelle concentration on the stability of metal-5-hydroxysalicylic acid complex species can be seen in Figure 1. When the concentration of micelles increases as predicted, the stability of complex species increases as a result of a decrease in the dielectric constant of the system and an increase in the concentration of micelles. According to previous studies[30,31] and Born's equation,[32] electrostatic contacts affect the dielectric constant of the system. The shift in stability of 5-HSA metal complexes in the presence of CTAB indicates that electrostatic forces predominate over non-electrostatic forces. In case of metal complexes with CTAB composition, divergence in linear stability change could be caused by co-solvent effects like water exposure, specific interactions or ionic stabilizing nature. The influence of a solvent is examined at the molecular level in this study.[33-35]

## Distribution Diagrams

5-hydroxysalicylic acid possesses three protons that can dissociate, making it capable of producing $LH_3$ at low pH and $LH_2^-$ and $LH^{2-}$ at higher pH. Since the second hydroxyl group deprotonates at very high pH, measuring its deprotonation equilibrium with a glass electrode is inaccurate.

The two groups i.e., carboxyl and hydroxyl present in the 5-Hydroxysalicylic acid ($LH_3$) are ionizable. In the pH ranges 1.4-4.0, 2–11.0, and > 10.0, the active forms of 5-HSA are $LH_3$, $LH_2^-$, and $LH^{2-}$, respectively. For all three metal ions, $ML_2H$, $ML_2H_2$, and $ML_3H_3$ complexes are predicted in this study. The

**Table 3: The effect of mistakes in the influencing components on $Ca^{II}$-5-hydroxysalicylic acid complexes in a 0.5% w/v CTAB-aqueous system.**

| Component | % Error | log $\beta_{mlh}$(SD) | | |
|---|---|---|---|---|
| | | $ML_2H_3$ | $ML_2H_4$ | $ML_3H_4$ |
| | 0 | 32.92(16) | 34.99(15) | 46.26(14) |
| Acid | -5 | Rejected | Rejected | Rejected |
| | -2 | 31.28(38) | Rejected | 44.85(49) |
| | +2 | 34.26(32) | 36.60(41) | 47.02(44) |
| | +5 | Rejected | Rejected | Rejected |
| | -5 | Rejected | Rejected | Rejected |
| | -2 | 34.61(39) | 36.81(39) | 47.10(45) |
| Alkali | +2 | 18.56(72) | 28.45(69) | 42.33(43) |
| | +5 | Rejected | Rejected | 42.72(82) |
| | -5 | Rejected | Rejected | Rejected |
| | -2 | 32.54(36) | 34.61(25) | 46.44(24) |
| Ligand | +2 | 32.26(26) | 35.33(25) | 46.54(24) |
| | +5 | Rejected | Rejected | 42.82(91) |
| Metal | -5 | 32.91(18) | 35.09(16) | 46.33(17) |
| | -2 | 32.92(17) | 35.03(16) | 46.26(15) |
| | +2 | 32.92(16) | 34.95(16) | 46.22(14) |
| | +5 | 32.91(19) | 34.89(18) | 46.17(16) |
| | -5 | 32.82(20) | 34.91(19) | 46.22(19) |
| Volume | -2 | 32.92(16) | 34.99(16) | 46.26(15) |
| | +2 | 32.92(17) | 34.99(16) | 46.26(14) |
| | +5 | 32.72(18) | 34.90(16) | 46.36(16) |
| | -5 | 32.92(19) | 34.99(18) | 46.26(18) |
| Log F | -2 | 32.92(17) | 34.99(16) | 46.26(16) |
| | +2 | 32.92(17) | 34.99(16) | 46.26(15) |
| | +5 | 32.92(18) | 34.99(16) | 46.26(16) |

following are the possible complex equilibria of 5-HSA with Ca, Mg, and Zn divalent metal ions.

Figure 2 shows distribution diagrams for different types of 5-HSA acid with divalent calcium, magnesium and zinc ions. The plots reveal that 5-HSA produces calcium and magnesium complexes with divalent ions at pH values ranging from 1.5 to 10.0, and zinc complexes at pH values ranging from 1.5 to 9.0. The pH range specified produces $ML_2H_3$, $ML_2H_4$ and $ML_3H_4$ species.

In comparison to $ML_2H_4$, $ML_2H_3$ and $ML_3H_4$ complexes are seen at high pH, which is shown in Table 4. $ML_2H_3$ is formed when $ML_2H_4$ species are deprotonated. It is observed that with an increase in pH ranging from 4-10.0 for Ca(II) and Mg(II) the concentrations of $ML_3H_2$ and $ML_3H_4$ species decreased simultaneously. In the instance of Zn(II), it is observed that with an increase in pH ranging from 5-9.0 the concentrations of $ML_3H_2$ and $ML_3H_4$ species decreased simultaneously. The formation of more $ML_2H_4$ species in the presence of Zn(II) than Ca(II) and Mg(II) was observed.

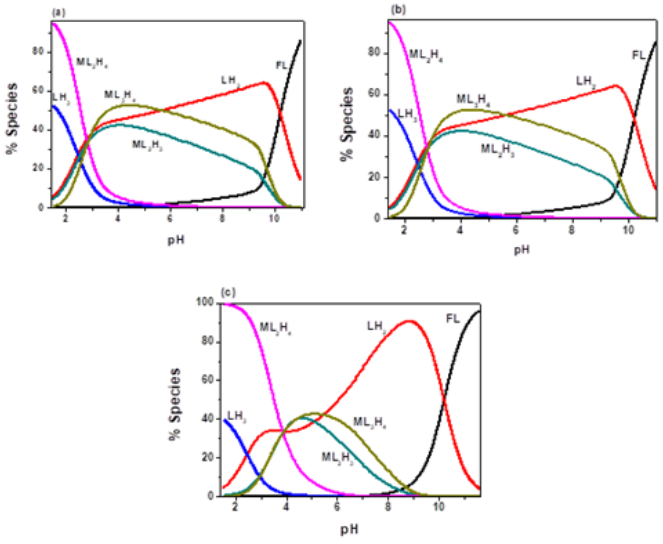


**Figure 2:** 5-Hydroxysalicylic acid binary complex patterns in a CTAB-water system of 1.0% w/v: (a) $Ca^{II}$, (b) $Ma^{II}$, and (c) $Zinc^{II}$.

**Table 4: Possible Metal-ligand chemical equilibria.**

| | | | |
|---|---|---|---|
| $M(II) + LH_3$ | ⇌ | $MLH_2^+ + H^+$ | (1) |
| $MLH_2^+$ | ⇌ | $MLH + H^+$ | (2) |
| $M(II) + LH_2^-$ | ⇌ | $MLH + H^+$ | (3) |
| $M(II) + LH_3$ | ⇌ | $MLH + 2H^+$ | (4) |
| $M(II) + 2LH_3$ | ⇌ | $ML_2H_4 + 2H^+$ | (5) |
| $ML_2H_4$ | ⇌ | $ML_2H_3^- + H^+$ | (6) |
| $M(II) + 2LH_2^-$ | ⇌ | $ML_2H_2^{2-} + 2H^+$ | (7) |
| $ML_2H_4$ | ⇌ | $ML_2H_2^{2-} + 2H^+$ | (8) |
| $M(II) + 2LH_3$ | ⇌ | $ML_2H_2^{2-} + 4H^+$ | (9) |
| $M(II) + 3LH_3$ | ⇌ | $ML_3H_6^- + 3H^+$ | (10) |
| $ML_3H_6^-$ | ⇌ | $ML_3H_4^{3-} + 2H^+$ | (11) |
| $ML_3H_6^-$ | ⇌ | $ML_3H_3^{4-} + 3H^+$ | (12) |
| $M(II) + 3LH_2^-$ | ⇌ | $ML_3H_3^{4-} + 3H^+$ | (13) |
| $M(II) + 3LH_3$ | ⇌ | $ML_3H_3^{4-} + 6H^+$ | (14) |
| $M(II) + 3LH_3$ | ⇌ | $ML_3H_4^{3-} + 5H^+$ | (15) |

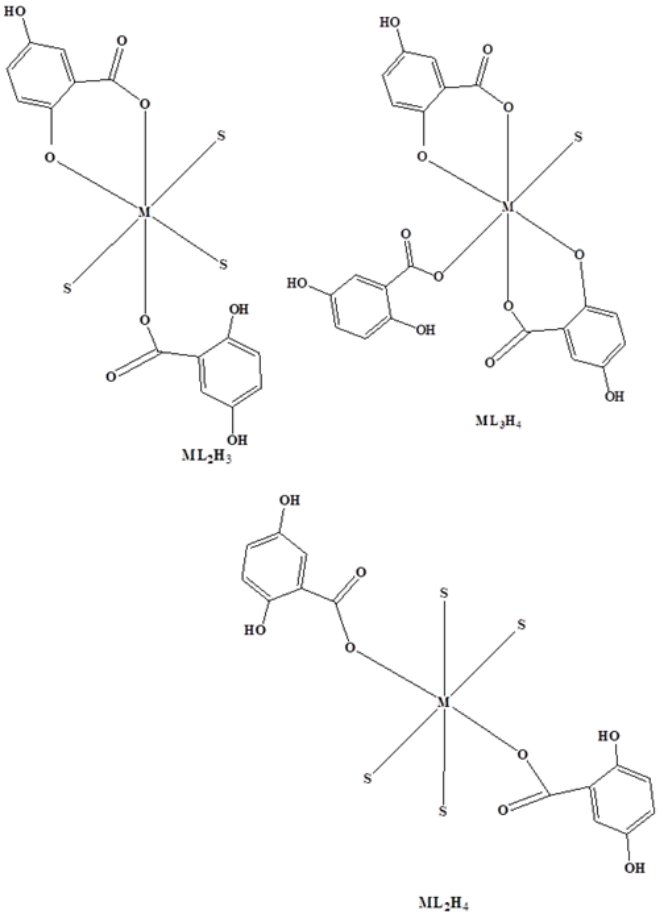


**Figure 3:** The structure of complexes containing 5-hydroxysalicylic acid in which S represents either solvent or water molecules.

## Structures of Metal Complexes

The binary complexes formation in 5-hydroxysalicylic acid takes place the participation of two oxygen sites, resulting in the more stable rings. The proposed structures for all metal ions are octahedral in this study. As six electron pairs are available, the divalent calcium, magnesium, and zinc ion complexes should be octahedral according to the valence shell electron pair repulsion hypothesis, as seen in Figure 3.

## CONCLUSION

In the pH range 2.0-10.5, 5-hydroxysalicylic acid forms complexes with metal ions of calcium, magnesium and zinc, which divalent. The metal ligand complexes formed in the present study are $ML_2H_3$, $ML_2H_4$, and $ML_3H_4$. It is observed that there is a measurable change in the stability constants of the metal complexes with respective to CTAB composition; it describes the predominant role of electrostatic forces. As the concentration of CTAB is increasing, the $log_{mlh}$ values of Ca(II), Mg(II) and Zn(II) complexes were increased. Stabilization and destabilization of species are caused by electrostatic interactions and a decreasing dielectric constant. The stability of reactant modified complexes is in the order alkali component > acid component > ligand component > metal component > total volume component > log F component. This study contributes to our understanding of the interactions between metals and ligands in aqueous-organic solvent combinations and has the potential to be extremely instructive for future research on medicinal applications.

## ACKNOWLEDGEMENT

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**5-HSA:** 5-Hydroxysalicylic acid; **CTAB:** Cetyltrimethylammonium Bromide; **MLH:** Metal Ligand Hydrogen; **Ca(II):** Calcium(II); **Mg(II):** Magnesium(II); **Zn(II):** Zinc(II); **EDTA:** Ethylene Diamine Tetra Acetic acid; **HCl:** Hydro Chloric acid; **DMSO:** Dimethyl Sulfoxide.

## SUMMARY

Chemical Speciation/Speciation analysis is a vital study to determine the concentrations of an individual metal ion and its molecular forms in human biology and toxicology, as the changes or variations in their concentrations and forms leads to toxicity and biological disorders. In the present study the author has studied the chemical speciation of Ca(II), Mg(II) and Zn(II) with 5-Hydroxysalicylic acid as the above mentioned metal ions plays crucial role in metabolism and changes in their concentrations leads to metabolic disorders. C-TAB is selected in these studies to maintain the dielectric properties of the medium in comparable levels to those of the physiological fluids. The present study provides wide knowledge on type of complexes formed, stability of complexes, and effect of acid, base, and metal and ligand concentrations on stability constants. The pH meter is used for titrations and SCPHD amd MINIQUAD 75 software's are used to obtain the statistical data in order to understand the metal-ligand complex behavior. The behavior of the drug with metal ions can be easily understandable with the obtained results. The species refined and their relative concentrations under the present experimental conditions represent the possible forms of metal ions in the biological fluids. Further, computer augmented modeling studies were carried out to arrive at the best fit chemical models and to check their validity.

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