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SYNTHESIS, CHARACTERIZATION, EQUILIBRIUM AND BIOLOGICAL STUDIES OF NOVEL 33-(1-(BENZO[D]THIAZOL-2-YLIMINO)ETHYL)-6-METHYL-2H-PYRAN-2,4(3H)-DIONE AND ITS Cu (II), Ni (II) AND Hg (II)METAL COMPLEXES: AN EXPERIMENTAL AND THEORETICAL APPROACH

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Keywords:

3BTIEMPD,
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ABSTRACT: The compound 3-(1-(benzo[d]thiazol-2-ylimino) ethyl)-6-methyl-2H-pyran-2, 4(3H)-dione (3BTIEMPD) and its metal complexes were prepared and characterized by spectro-analytical techniques. Irving-Rossetti pH-metric technique was employed to determine the number of dissociable protons and chelation sites of the title compound. Hyper Chem 7.5 software was used to understand donor and acceptor properties of molecule. The molecule was built and the geometry optimization was carried out by using semiemperical PM3 method. The contour maps of highest occupied molecular orbitals (HOMO) and lowest unoccupied molecular orbitals (LUMO) and corresponding binding energy values were computed. The low binding energy for ionic species evident from computed values is an indication of higher possibility of compound to bind with metal ions through deprotonation. This is augmented from the results of spectro-analytical analyses of isolated solid metal complexes wherein the participation of azomethine nitrogen and the enol oxygen of pyran ring through deprotonation is envisaged. All the compounds were investigated for their antimicrobial activities against the Gram-positive and Gram-negative bacteria by disc diffusion method. It was found that the antibacterial activity of Hg (II)-3BTIEMPD is dominant over standard ampicillin.

INTRODUCTION: Over the past four decades heterocyclic compounds were reported to have wide-range of biological applications and are still of great scientific interest till today. Heterocycles are an important class of compounds, which have been frequently found as a key structural unit in synthetic pharmaceuticals and agrochemicals.

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Among the heterocyclic compounds which act as drugs, benzothiazole based pharmaceuticals possess multiple applications [1-3]. The review of literature reveals that, the benzothiazole moiety was an important scaffold in the development of drugs and it also shows good biological activities such as antibacterial [4], anticancer [5, 6], antitumor [7], anti-microbial, anti-inflammatory [8] and antifungal activities [9].

Substituted benzothiazoles like 2-aminobenzothiazoles and their derivatives were found to have wide range of applications [10-12]. An interest has been focused on the common chemotherapeutic activity of oxygen containing heterocyclics such as 2-pyran which acts as cytotoxic agent against some human cancer cell lines [13].

Keeping in view the potential biological activity of 2-aminobenzothiazoles, in the present investigation it has been planned to combine both 2-aminobenzothiazole and a 2-pyran derivative viz., dehydroacetic acid (DHA) in one molecular frame to enable the formation of corresponding imine base. DHA is one of the most important oxygen heterocyclic with various active functional groups, which acts as an excellent complexing agent [14, 15] and also possesses diverse biological applications.

Transition metal ions play an important role in biological systems and often form stable metal complexes with O, N and O, O donor atoms. Coordination chemistry of transition metal ions is the most widely developed field [16, 17] with their metal complexes, exhibiting wide-ranging properties and relevant applications in various fields [18, 19]. Metal complexes of imine bases are found to be of great interest in coordination chemistry [20-22] as the biological activity of an imine base sometimes may increase profoundly upon coordination. Considering the importance of DHA and 2-aminobenzothiazole in various fields we have synthesized novel 3-(1-(benzo[d]thiazol-2-ylimino) ethyl)-6-methyl-2H-pyran-2, 4(3H)-dione (3BTIEMPD) and its metal complexes. These were characterized by various spectro-analytical techniques such as mass, IR, UV-Visible, NMR, SEM, EDX, ESR, TGA and DTA. Further their antibacterial studies were explored to anticipate future plan for *in vivo* and *in vitro* studies.

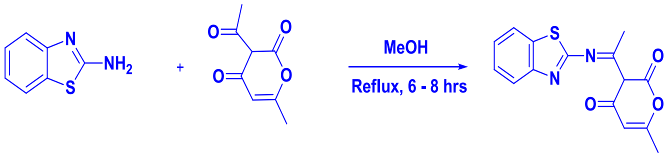
MATERIALS AND METHODS:

Physical measurements: All chemicals used are of AR grade. Dehydroacetic acid and 2-amino Benzothiazole of Merck grade were used as supplied. Metal chlorides [$CuCl_2.2H_2O$, $NiCl_2.6H_2O$ and $HgCl_2$] and solvents were purchased from E- Merck and A.R grade. The pH measurements were made using a digital ELICO electronic model LI 120 pH meter in conjunction with a combined glass and calomel electrode. The pH meter was calibrated at different pH values 7.0, 4.0 and 9.2 using the appropriate standard buffers with necessary temperature corrections. Melting points were measured on Cintex melting point apparatus. Mass spectra were recorded on Shimadzu Qp 5050A. FT-IR spectra (4000–400 cm^{-1}) of the free ligand and complexes were recorded as KBr pellets on Perkin-Elmer 337 spectrophotometer. The UV–Visible spectra of the 3BTIEMPD and metal complexes were recorded in the wavelength range (200-900 nm) on Shimadzu UV-VIS spectrophotometer.

The NMR spectra were recorded in MeOH with Bruker 400 MHz instrument using TMS as internal reference. Magnetic susceptibility measurements of transition metal complexes were determined on a Guoy balance at room temperature using Hg [Co $(SCN)_4$] as standard. Thermal analysis of complexes was performed on Shimadzu DTG-50H analyzer under nitrogen atmosphere from room temperature to 1000 °C at a heating rate of 20 °C/min. The micro-morphology and distribution of elemental components in the samples were analyzed on Zeiss Scannig Electron Microscope (SEM), with an energy dispersive analysis system of X-ray spectrometer (EDX). EPR spectra of powdered samples were recorded on E-112 Varian model instrument in X-band using DPPH as an internal standard. The computational studies were carried out by using HyperChem7.5 software.

Synthesis of 3BTIEMPD:

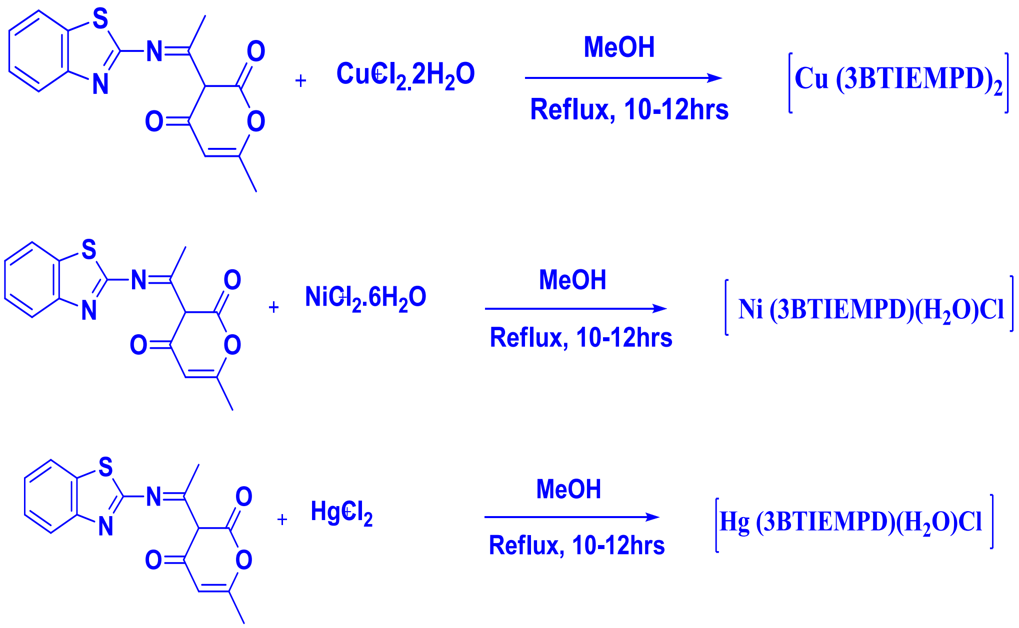
0.66mmol of benzo[d]thiazol-2-amine, 0.66mmol 3-acetyl-6-methyl-2H-pyran-2,4(3H)-dione and absolute methanol are taken in a 100 ml round bottomed flask, to this mixture 2-3 drops of acetic acid was added, the resulting mixture was heated at 60 - 65 °C under magnetic stirring for 6 – 8 hrs. Reaction was monitored by TLC. After completion of reaction, the reaction mixture was cooled and poured on to ice cold water (30 ml). The separated solid was filtered, washed with petroleum ether, recrystallized and dried under vacuum over night (Yield = 87% and m.p 220-230 °C).



SCHEME 1 SYNTHESIS OF 3BTIEMPD

Synthesis of metal complexes:

To a stirred hot ethanolic solution of 3BTIEMPD (0.02mmol), metal chlorides of Cu (II), Ni (II) and Hg (II) in absolute methanol (3.6 ml) was added drop wise at room temperature. To this solution few drops of 5% alcoholic ammonia was added and the pH of the resulting solution was adjusted to 7.0. Then the reaction mixture was refluxed on a magnetic stirrer continuously for10-12 hrs at 60-65 °C. Precipitate obtained was filtered by suction and purified by washing several times with distilled water, hot ethanol followed by ether. The pure complex was dried in a desiccator over anhydrous calcium chloride at room temperature. (Yield =73% and m.p > 300 °C).



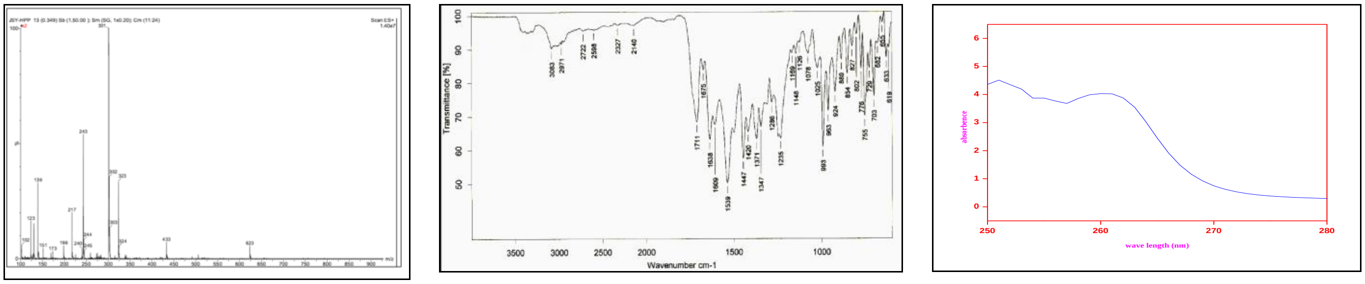
SCHEME 2: SYNTHESIS OF METAL COMPLEXES

RESULTS AND DISCUSSION:

Structure and characterization of 3BTIEMPD:

Mass, IR and UV-Visible spectra:

The mass spectrum of the ligand exhibits a dominant base peak at m/z 301and the spectrum also shows a peak at m/z 323 which corresponds to sodium adduct. The IR spectrum of 3BTIEMPD shows characteristic band at 1711-1675 cm^{-1} assignable to ν (C=O) pyran lactone and the three strong bands in the frequency range of 1638 cm^{-1} ,1609 cm^{-1} and 1539 cm^{-1} corresponds to pyran carbonyl ν (C=O), azomethine ν (C=N) and aromatic ring ν (C=N) vibrations respectively [33]. Aromatic stretching ν (C=C) vibrations appeared at 1447–1235 $cm^{-1}$and the bands at 1148 cm^{-1} , 3083 $cm^{-1}$and 2971 cm^{-1} are ascribable to (C-O-C), aromatic ν (C-H) and aliphatic ν (C-H) stretching vibrations respectively. The UV-Visible spectrum of 3BTIEMPD showed two peaks at wavelengths of 265nm and 285 nm assignable to n→ π* (C=O) and π→ π* (C=C) transitions respectively (**Fig.1a, 1b & 1c**).



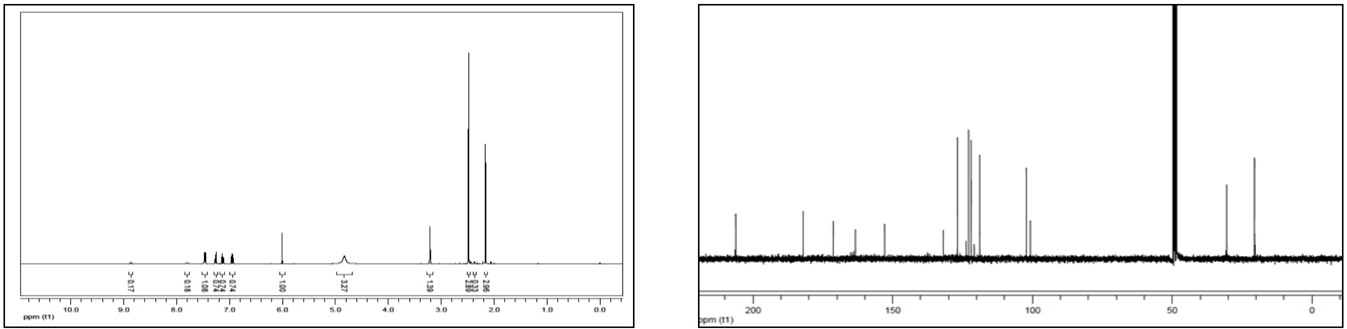
a) MASS SPECTRUM b) IR SPECTRUM c) UV-VISIBLE SPECTRUM

FIG. 1: MASS, IR AND UV-VISIBLE SPECTRA OF 3BTIEMPD

NMR spectra:

The ^{1}H-NMR spectrum of 3BTIEMPD is recorded in MeOH (**Fig. 2a**). The phenyl ring protons appeared as a multiplet within the range of 6.90 - 7.60 (m, 4H) ppm. The peaks recorded at δ 2.20 (s, 3H) and δ 2.53 (s, 3H) ppm are assignable to the aliphatic protons. The (HC = C) proton is observed as a single within the range of 6.00 ppm and the active methylene (CH) proton of pyran ring is recoded at δ 3.20 (s, H) ppm [33].

^{13}C-NMR spectrum of 3BTIEMPD is recorded in MeOH (**Fig.2b**). The aromatic carbons are recorded at δ 120-153 ppm, aliphatic carbons appeared at δ 20-30 ppm, the peaks at δ 206 and δ 182 ppm corresponds to carbonyl carbon of pyran ring. Azomethine carbons are observed at δ161, 170 ppm and the peak at δ 100-105 ppm is assignable to alkenyl (C = C) carbons [33].



a) ^{1}H-NMR b) ^{13}C-NMR

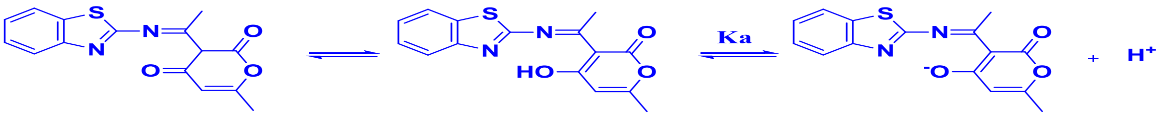
FIG. 2: ^{1} H-NMR AND ^{13}C-NMR SPECTRA OF 3BTIEMPD

pH-Metric studies:

To know the potential binding sites and chelation properties of the ligand an attempt was made to determine dissociation constants by employing Irving-Rossetti pH-metric technique [26, 27].

The pH-metric titrations with 3BTIEMPD in 70% DMF medium also inferred dissociation of one proton. From the titration curves and structural properties of candidate compound, it can be envisaged that the enolic proton is released from pyran ring corresponding to the pKa value of 5.40 (**Fig. 3 a & b**). In the presence of Cu^{2+} ion the proton is released more easily as metal ion competes for binding.

Keto- Enol tautomerism and the dissociation of proton in 3BTIEMPD.



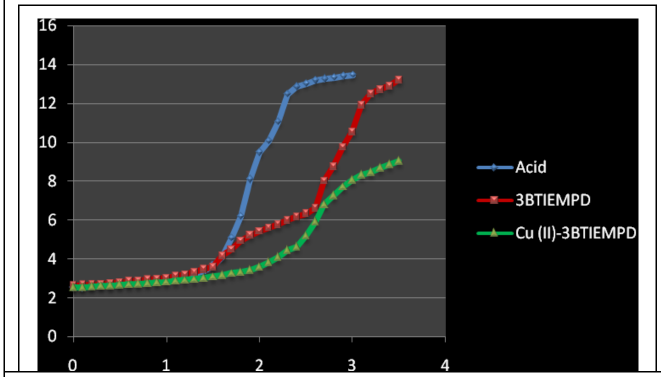


FIG.3A: pH METRIC TITRATION CURVE OF 3BTIEMPD IN 70%v/v DMF MEDIUM AT 303K AND 0.1 KNO_3 IONIC STRENGTH

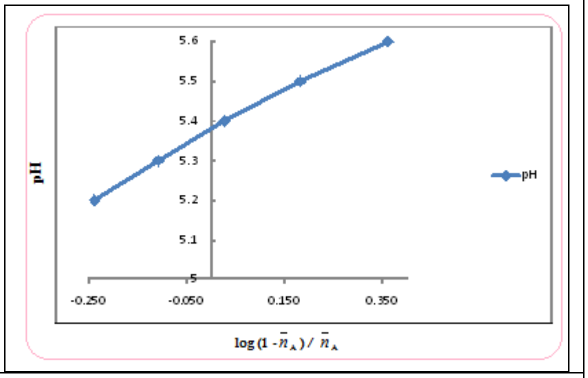


FIG.3B: PLOTS OF LOG (1 - $\bar{n}_A$) / $\bar{n}_A$ Vs pH OF 3BTIEMPD IN 70% v/v DMF - WATER MEDIUM

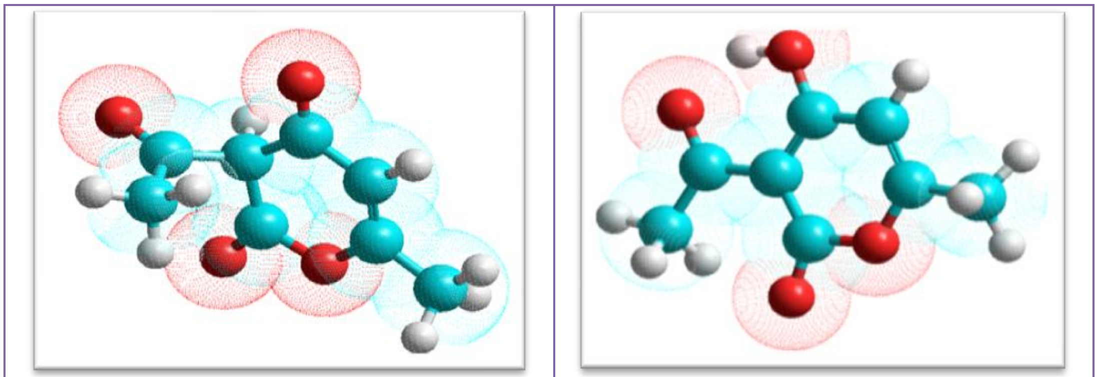
From these studies it is also evident that, though keto–enol tautomerism exists in 3BTIEMPD, release of proton from the enol form is more feasible because of its resonance stabilized structure. Our experimental studies established that coordination of 3BTIEMPD to the metal ions is facilitated through deprotonation from enol form rather than keto form.

Computational studies: Quantum chemical calculations have been extensively used to study donor and acceptor properties of molecule. By using Hyper Chem 7.5 software [23, 24] the molecule was built, the geometry optimization and the molecular orbital calculations were performed by employing semi-empirical PM3 method [25] to understand donor and acceptor properties of molecule. For a small and medium sized molecule semi-empirical method is the most suitable method.

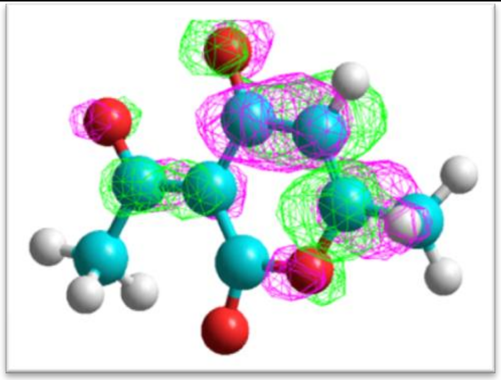
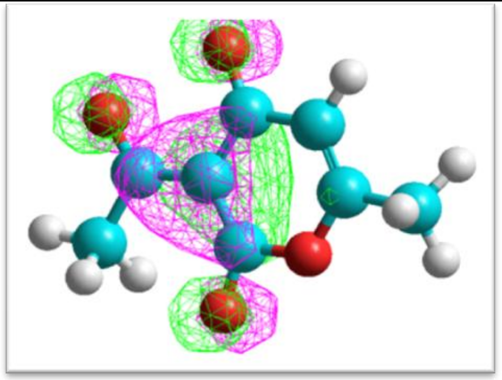
In general the reactivity of the compound is majorly dependent on the energy difference between the energy levels of E_{HOMO} and E_{LUMO}. In the present investigation we focused mainly on the energy calculations of the frontier molecular orbitals.

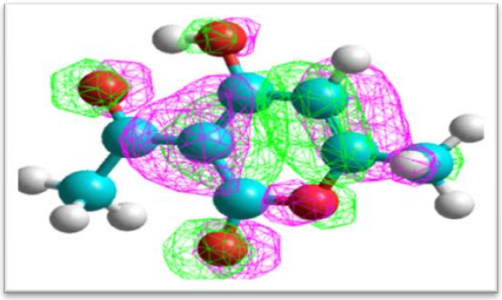
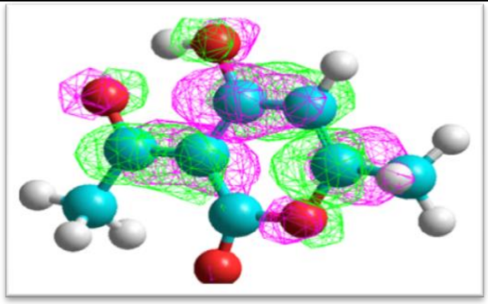
The title compound being one of the analogue of DHA and the core structural unit in 3BTIEMPD is pyran moiety, the frontier orbitals were computed for both 3BTIEMPD and DHA. Since both molecules exist in keto and enol forms, the geometry optimization was done in both forms and the properties of frontier orbitals were compared in respective systems (**Fig.4** and **5**). The energy gap between the E_{HOMO} and E_{LUMO} orbitals for keto, enol and ionized forms of DHA and 3BTIEMPD were shown in (**Table 1**).

Orbital properties of DHA:



(Keto form)	**(Enol form)**
a)Geometry Optimized Structure of DHA	

Keto Form	
	
Contour map of HOMO **Binding Energy: +10.550 eV**	**Contour map of LUMO** **Binding Energy: +0.923 eV**

Enol Form	
	
Contour map of HOMO **Binding Energy: +9.710 eV**	**Contour map of LUMO** **Binding Energy: +1.150 eV**
b) Highest occupied molecular orbitals (HOMO) and Lowest unoccupied molecular orbitals (LUMO) of DHA (Keto Form) & (Enol Form)	

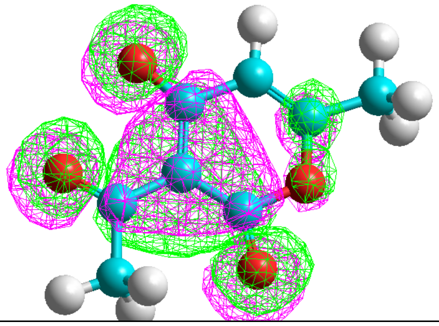
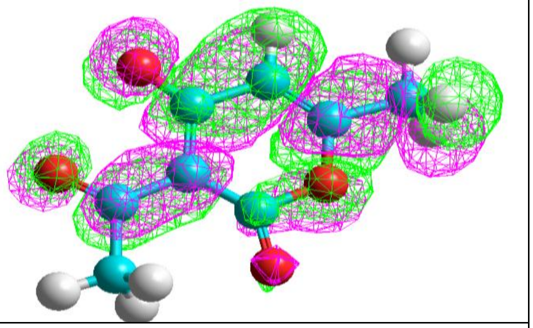
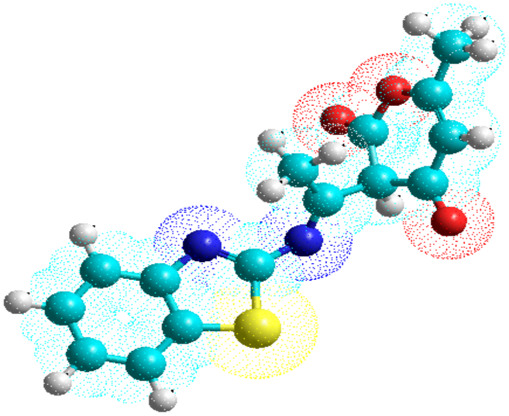
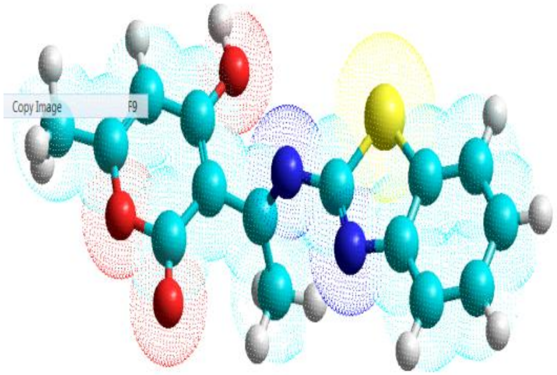
Ionized Form	
	
Contour map of HOMO **Binding Energy: 4.351eV**	**Contour map of LUMO** **Binding Energy: -4.001 eV**
c) Highest occupied molecular orbitals (HOMO) and Lowest unoccupied molecular orbitals (LUMO) of DHA (Ionized Form)	

FIG. 4: a) GEOMETRY OPTIMIZED STRUCTURE, b) HIGHEST OCCUPIED MOLECULAR ORBITALS (HOMO) AND LOWEST UNOCCUPIED MOLECULAR ORBITALS (LUMO) OF DHA (KETO FORM) & (ENOL FORM) AND c) HIGHEST OCCUPIED MOLECULAR ORBITALS (HOMO) AND LOWEST UNOCCUPIED MOLECULAR ORBITALS (LUMO) OF DHA (IONIZED FORM)

Orbital properties of 3BTIEMPD:

	
(Keto form)	**(Enol form)**
a) Geometry Optimized Structure of 3BTIEMPD	

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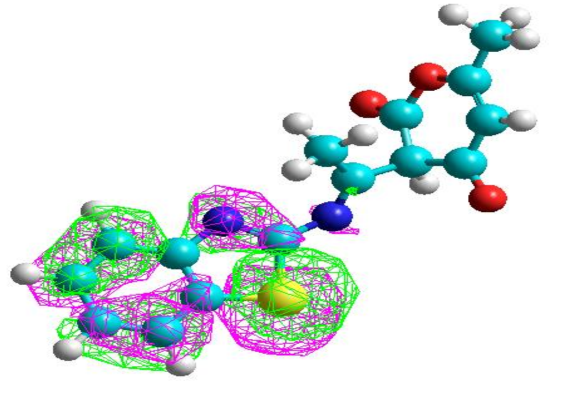
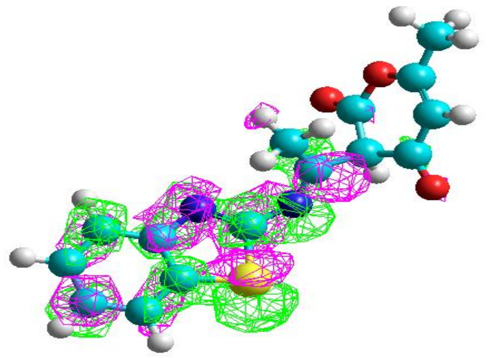
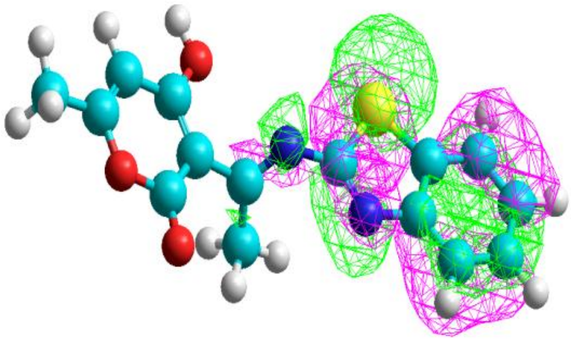
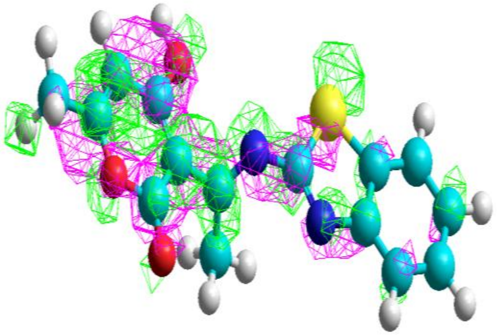
<tr><th colspan="2">Keto Form</th></tr>
<tr><td></td><td></td></tr>
<tr><td>Contour map of HOMO
Binding Energy: +9.247eV</td><td>Contour map of LUMO
Binding Energy: +1.015eV</td></tr>
<tr><th colspan="2">Enol Form</th></tr>
<tr><td></td><td></td></tr>
<tr><td>Contour map of HOMO
Binding Energy: +9.028 eV</td><td>Contour map of LUMO
Binding Energy: +0.996 eV</td></tr>
<tr><td colspan="2">b) Highest occupied molecular orbitals (HOMO) and Lowest unoccupied molecular orbitals (LUMO) of 3BTIEMPD (Keto Form) & (Enol Form)</td></tr>
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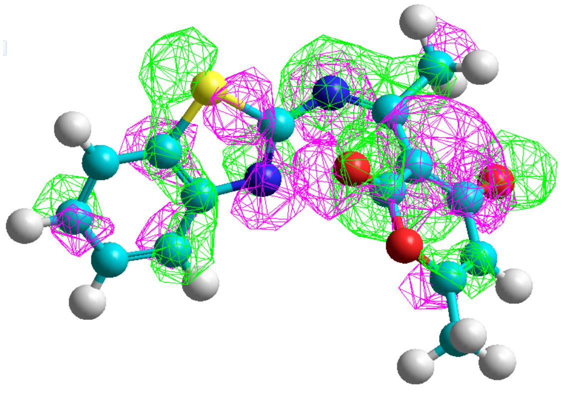
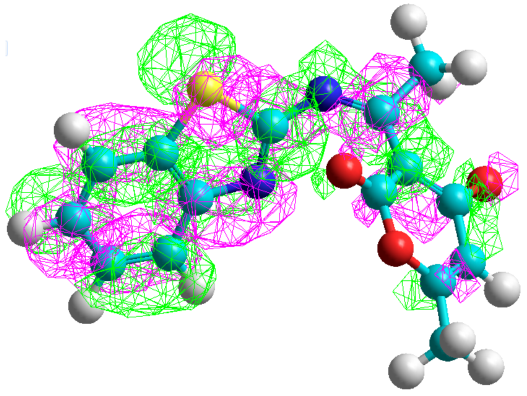
<tr><th colspan="2">Ionized Form</th></tr>
<tr><td></td><td></td></tr>
<tr><td>Contour map of HOMO
Binding Energy: 4.630 eV</td><td>Contour map of LUMO
Binding Energy: -2.423 eV</td></tr>
<tr><td colspan="2">c) Highest occupied molecular orbitals (HOMO) and Lowest unoccupied molecular orbitals (LUMO) of 3BTIEMPD (Ionized Form)</td></tr>
</table>

FIG. 5: a) GEOMETRY OPTIMIZED STRUCTURE, b) HIGHEST OCCUPIED MOLECULAR ORBITALS (HOMO) AND LOWEST UNOCCUPIED MOLECULAR ORBITALS (LUMO) OF 3BTIEMPD (KETO FORM) & (ENOL FORM)   c) HIGHEST OCCUPIED MOLECULAR ORBITALS (HOMO) AND LOWEST UNOCCUPIED MOLECULAR ORBITALS (LUMO) OF 3BTIEMPD (IONIZED FORM)

TABLE 1: ENERGY DIFFERENCE BETWEEN E_{HOMO} and E_{LUMO} OF DHA AND 3BTIEMPD

Structural Form	DHA			3BTIEMPD		
	E_{HOMO}	E_{LUMO}	E_{HOMO} - E_{LUMO}	E_{HOMO}	E_{LUMO}	E_{HOMO} - E_{LUMO}
Keto Form	10.55	0.92	9.62 eV	9.24	1.01	8.19 eV
Enol Form	9.71	1.15	8.56 eV	9.02	0.99	8.02 eV
Ionized Form	4.35	-4.00	8.35 eV	4.63	-2.42	7.05 eV

The title compound being monobasic acid as evident from pH-metric studies discussed earlier, the frontier orbitals were also computed for its ionized form. The computed value of E_{HOMO} and the energy difference between E_{HOMO} and E_{LUMO} are less in ionzed form compared to corresponding values in keto and enol forms of 3BTIEMPD, which infers enhanced electron donor properties of ionic form. Both pH-metric and computational studies of current investigation support binding of metal ion with title compound in ionized form.

Spectrophotometric studies:

Job's continuous variation method:

To corroborate the composition of metal complex formation an attempt was made to determine the metal to ligand stoichiometric ratio in Cu (II)-3BTIEMPD system, employing jobs method of continuous variation [32]. A series of Cu (II) and 3BTIEMPD solutions were prepared with identical concentrations (0.001M). They were mixed in different volumes keeping total volume of the mixture constant. pH of the solutions was adjusted using acetate buffer solution. The absorbance of each solution was measured at 508 nm and a graph was plotted between absorbance and mole fraction of ligand. From the graph it is conspicuous that metal to ligand ratio corresponds to 1:2 stoichiometry (**Fig.6**).

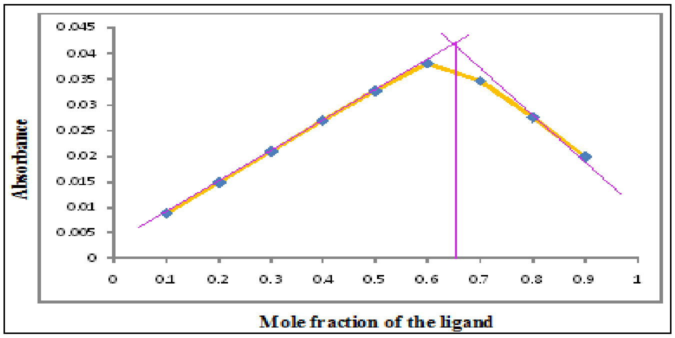
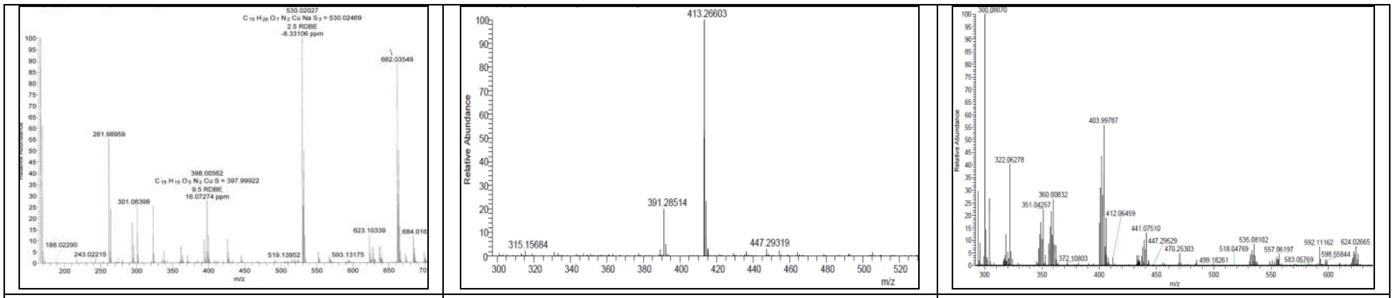


FIG.6: THE PLOT OF ABSORBANCE vs MOLE FRACTION OF THE LIGAND AT 303 K IN DMF MEDIUM

Structure and characterization of metal complexes:

Mass spectra: The mass spectrum of the Cu (II)-3BTIEMPD complex showed a peak at m/z 662 (**Fig.7a**). From the mass spectrum it is apparent that the expected mass is in accordance with the formation of metal complex in 1:2 ratio. While the mass spectrum of the Ni (II)-3BTIEMPD (**Fig.7b**) complex exhibited a dominant base peak at m/z 413 and Hg (II) metal complex (**Fig.7c**) a quasi ion peak at m/z 557, ascertaining 1:1 stoichiometry of metal ligand composition for both complexes.



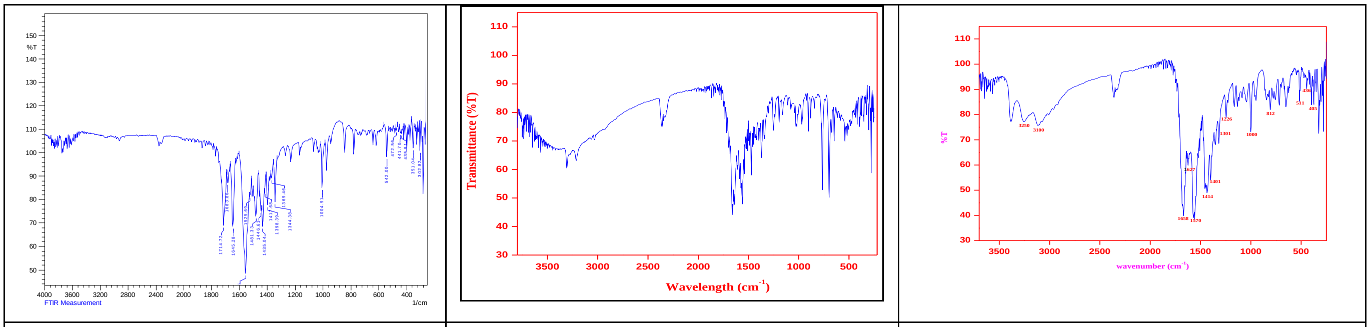
a) Cu (II)-3BTIEMPD	b) Ni (II)-3BTIEMPD	c) Hg (II)-3BTIEMPD

FIG. 7: MASS SPECTRA OF Cu (II), Ni (II) AND Hg (II) COMPLEXES

IR spectra:

IR spectrum of 3BTIEMPD was considered for comparison with IR spectra of metal complexes under study in order to elucidate structural variation in former compound upon chelate formation. The IR spectra of Ni (II) and Hg (II) metal complexes show characteristic band around 3305-3184 cm^{-1} corresponding to the presence of coordinated water which is further confirmed by the band at 837 cm^{-1}. The presence of coordinated water was also supported by TGA/DTA analysis of the complexes. The stretching frequency of pyran ν (C=O) is shifted from 1638 cm^{-1} to 1645 cm^{-1}, 1577 cm^{-1} and1658 cm^{-1} in Cu (II) ,Ni (II) and Hg (II) complexes respectively, which confirms that the carbonyl oxygen is coordinated to the metal ion [33]. The azomethine-nitrogen ν (C=N) vibration is shifted to 1525 cm^{-1},1529 cm^{-1} and1627cm^{-1} indicating the involvement of azomethine-nitrogen in the metal binding [33]. The ν (C-O) stretching vibrations also got ascended to 1004 cm^{-1}, 1132 cm^{-1} and 1000 cm^{-1} in Cu (II), Ni (II) and Hg (II) complexes respectively.

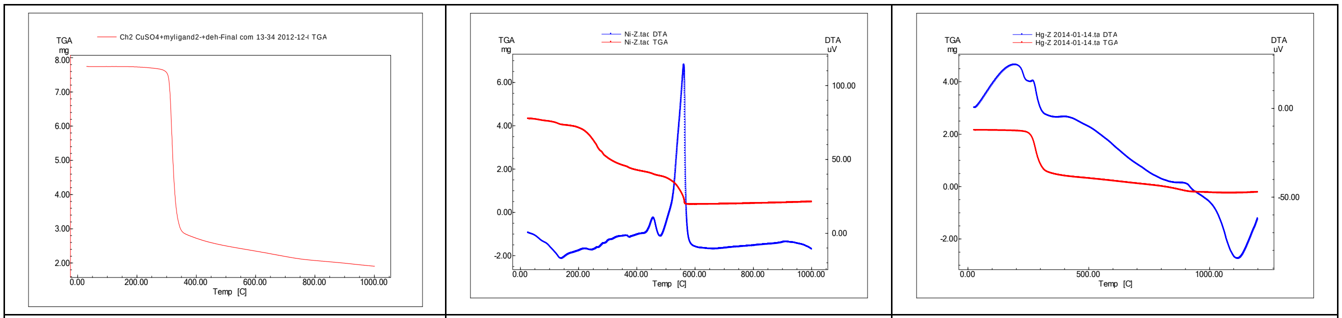
On complexation new bands appeared at 435 cm^{-1}, 432 cm^{-1}, 436 cm^{-1} and 542 cm^{-1}, 528 cm^{-1}, 511 cm^{-1} are assignable to stretching frequencies of M-N and M-O bonds [33]. From the FT-IR spectrum it is clear that the ligand 3BTIEMPD is coordinated to the metal centre via the oxygen of pyran ring and azomethine-nitrogen forming a six membered ring (**Fig. 8a, 8b & 8c).**



a) Cu (II)-3BTIEMPD **b) Ni (II)-3BTIEMPD** **c) Hg (II)-3BTIEMPD**

FIG. 8: IR SPECTRA Cu (II), Ni(II) AND Hg (II) COMPLEXES

Thermogravimetric analysis:



a) Cu (II)-3BTIEMPD **b) Ni (II)-3BTIEMPD** **c) Hg (II)-3BTIEMPD**

FIG. 9: THERMOGRAVIMETRIC ANALYSIS Cu (II), Ni (II) AND Hg (II)COMPLEXES

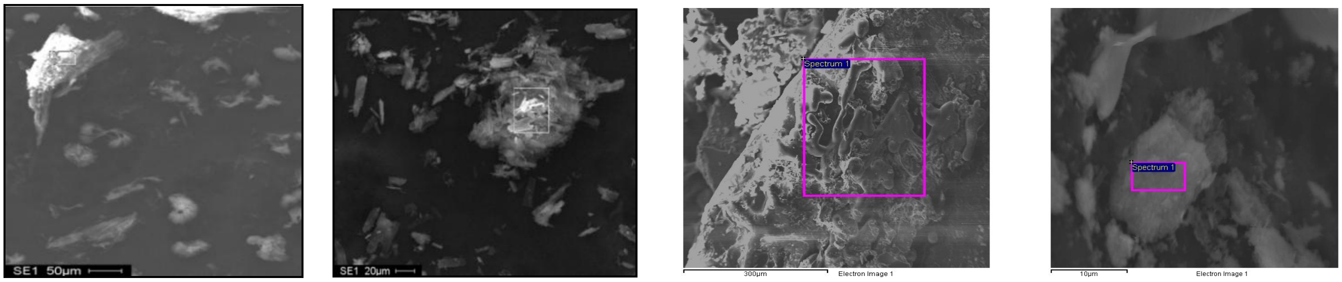
Thermogram of Cu (II) metal complex presented in Fig.9a reveals its thermal stability up to 220 °C and there after a steep slope in the range of 240-380 °C which may be attributed to removal of non coordinated part of the ligand [33]. Further decomposition in the range of 380-800 °C corresponds to the loss of total organic moiety.

The thermal decomposition curve of Ni (II) complex is shown in Fig.9b. From the TG/DTA curve it can be observed that the complex was stable up to 110 °C. The subsequent loss of weight up to 180 °C accompanied by appearance of endothermic peak in DTA curve corresponds to removal of coordinated water. Further decomposition in the temperature ranges 180-260 °C and 260-600 °C infers loss of ligand moiety in two steps. This loss of weight in two steps is accompanied by the release of energy as evident from two exothermic peaks in DTA curve indicates decomposition of nitrogen containing organic moiety with pyrolytic nature. The residual moiety is stable in the temperature range of 600-800 °C without further decomposition. A slight increase in the weight of residue above 800 °C is probably due to formation of metal oxide. Thermal degradation pattern of Hg (II) complex is presented in Fig.9c. The complex is stable up to 280 °C, and above this temperature the sudden weight loss in the region centered at 300 °C accompanied by exothermic peak in DTA curve is ascribable to simultaneous loss of both bound organic moiety as well as coordinated water. In the third step the slow gradual weight loss up to 700 °C indicates total decomposition of the complex. An endothermic peak beyond 1000 °C on DTA curve indicates melting of residual moiety.

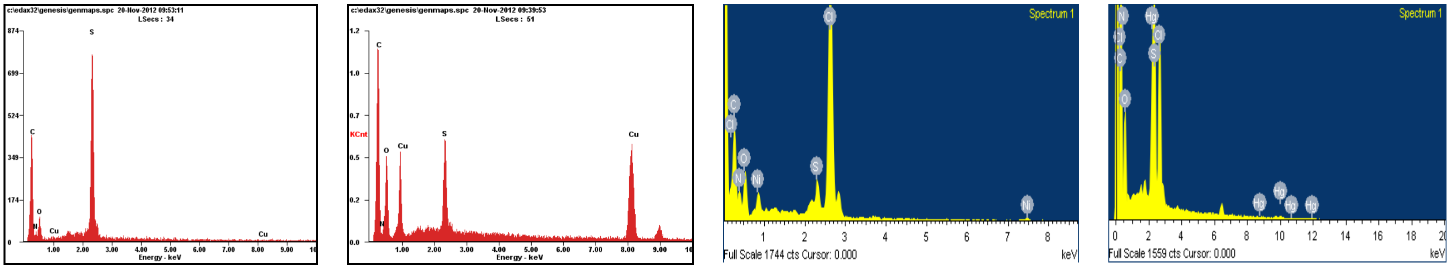
Scanning electron microscope and Energy-dispersive X-ray spectroscopy:

SEM provides detailed high resolution images of the sample by a focused electron beam across the surface and detecting secondary or backscattered electron signal. An Energy Dispersive X-Ray Analyzer (EDX) is used to provide elemental identification and quantitative compositional information [33].

The SEM analysis of title compound 3BTIEMPD elucidated its morphology wherein particle size recorded in specific region was 50µm. The SEM images of complexes of Cu (II), Ni (II) and Hg (II) with 3BTIEMPD displayed distinct morphologies with particle size of 20µm, 100µm and 10µm in respective systems (**Fig. 10a, 10b, 10c & 10d**). Further EDX data recorded confirmed its elemental composition (**Fig. 10e, 10f, 10g & 10h**).



a) **3BTIEMPD** **b) Cu (II)-3BTIEMPD** **c) Ni (II)-3BTIEMPD** **d) Hg (II)-3BTIEMPD**



e) 3BTIEMPD **f) Cu (II)-3BTIEMPD** **g) Ni (II)-3BTIEMPD** **h) Hg (II)-3BTIEMPD**

FIG. 10: SCANNING ELECTRON MICROSCOPE IMAGES AND ENERGY-DISPERSIVE X-RAY SPECTROSCOPY IMAGES OF 3BTIEMPD, Cu (II), Ni (II) and Hg (II) COMPLEXES

ESR spectrum:

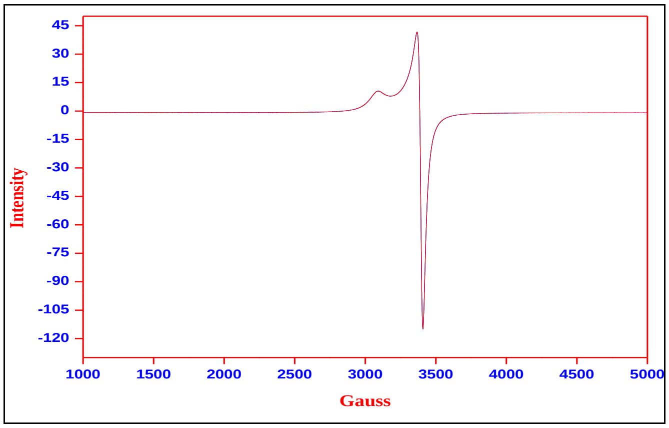


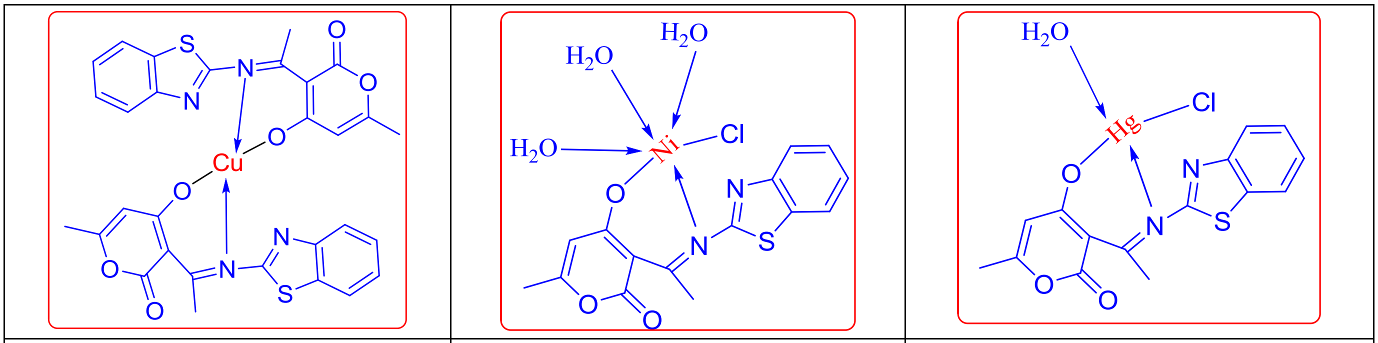
FIG.11: ESR SPECTRUM OF Cu (II)-3BTIEMPD

In general the ESR spectral features are important in understanding the geometry at metal center whether it is cubic or non cubic (axial or rhombohedral). The ESR spectrum of Cu (II)-3BTIEMPD complex (**Fig.11**) in solid state indicates three g values (g_x = 1.95, g_y = 1.922 and g_z = 2.13) confirming asymmetrical distribution of electron density and thus is an evidence to predict non cubic environment at metal ion centre in the complex. Though square planar structure is the possible geometry in present investigation (**Fig.12**), three g values indicate distorted axial symmetry in Cu (II)-3BTIEMPD complex.

Magnetic susceptibilities:

Guoy Balance was used to measure the magnetic susceptibilities of Cu (II), Ni (II) and Hg (II) at a room temperature. Cu (II) complex exhibited a magnetic momentum of 1.89 BM, Ni (II) complex shows a magnetic momentum of 2.55 BM and Hg (II) complex is diamagnetic.

Tentative structures of metal complexes:



Cu (II)-3BTIEMPD | Ni (II)-3BTIEMPD | Hg (II)-3BTIEMPD

FIG.12: TENTATIVE STRUCTURES OF METAL COMPLEXES

Antibacterial studies: The antibacterial studies were carried out on bacterial strains viz; *Bacillus subtilis*, *Klebsiella pneumonia*, *Staphylococcus aureus*, *Pseudomonas putida* and *Escherichia coli* by using disc diffusion method [33]. On the basis of the size of the zone of inhibition formed around the paper disks on the seeded agar plates the antibacterial activity was estimated in the units of millimeters. In general the antimicrobial activity is dependent on the permeability of lipid membrane that surrounds the cell favoring the passage of only lipid soluble materials. The results revealed that the antibacterial activity of 3BTIEMPD is more pronounced against two bacteria tested viz., *Bacillus subtilis* and *Klebsiella pneumonia* when compared to ampicillin standard. The activity of the 3BTIEMPD is however less than its metal complexes. Among the Ni (II), Cu (II) and Hg (II) complexes, Hg (II)-3BTIEMPD showed enhanced activity than ampicillin. Cu (II) and Ni (II) complexes also exhibited increased activity than ampicillin standard against the selected organism except for *Staphylococcus aureus*. The presence of dative bonds in metal chelates probably enhanced the cell permeable property thus making them more antimicrobial activity compared to the title compound (**Table 2).**

TABLE 2: COMPARING THE BIOLOGICAL ACTIVITY OF THE 3BTIEMPD AND ITS METAL COMPLEXES WITH THE STANDARD THE FOLLOWING RESULTS WERE OBTAINED.

Zone of Inhibition in (mm)						
S.No	**Name of Bacteria's**	**Cu(II) 3BTIEMPD**	**Ni(II) 3BTIEMPD**	**Hg(II) 3BTIEMPD**	**3BTIEMPD**	**Ampicillin**
1	Escherichia coli	9.3	9.6	13.4	3	5.6
2	Bacillus subtilis	8.7	7.2	11.3	6.1	5.2
3	Klebsiella pneumonia	8.1	10.3	14.2	9.2	8.1
4	Staphylococcus aureus	6.4	8.3	13.8	6.5	8.9
5	Pseudomonas putida	6.7	7.5	11.3	5	5.6

CONCLUSION: 3-(1-(benzo[d]thiazol-2-ylimino) ethyl) - 6 - methyl - 2H- pyran - 2, 4 (3H) – dione (3BTIEMPD) and its metal complexes were prepared and characterized by various spectro- analytical techniques. Irving-Rossetti pH-metric technique employed showed the presence of one dissociable proton. Computational studies reveal that enol form of the ligand is more reactive than keto form facilitating formation of metal complex through deprotonation. Equilibrium studies, FT-IR analysis along with other spectro-analytical techniques revealed that the azomethine nitrogen and the enol oxygen of pyran through deprotonation aid in the formation of metal complexes. Antimicrobial studies inferred more enhanced activity in complexes compared to in free ligand 3BTIEMPD. Among all complexes of present investigation, Hg (II)-3BTIEMPD showed highest activity. The studies were also informative to establish relatively high activity of complexes than with standard ampicilln towards the organism chosen and are also useful for planning further advanced *in vitro* and *in vivo* studies.

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