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Microwave assisted synthesis, Spectral characterization and Biological activities of Cu(II) complex with 2,4-thiazolidinedione and benzoate ion as Ligands

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Abstract: *A novel Cu(II) complex of 2,4-thiazolidinedione(TLD) and benzoate ion was synthesized by using microwave irradiation. Microwave synthesis gives a high yield of the complex within a short time. The molecular formula and the probable geometry of the complex have been deduced from elemental analysis, molar conductance, UV-Vis, FT-IR and EPR spectra. The molar conductance value indicates that the Cu(II) complex is non-electrolyte (1:0) type. FT-IR spectra show that 2,4- thiazolidinedione and benzoate ion are coordinated to the metal ion in a monodentate way. The metal ligand covalency of Cu(II) complex has been arrived from EPR spectrum. The geometry of the complex is found to be tetragonally distorted octahedral. The antimicrobial activities of the ligands and their Cu(II) complex are studied against the five bacteria (staphylococcus aureus, serratia, salmonella typhi, chromobacterium violaceum and burkolderia) and also two fungi (C.albicance and Aspergillus Niger) at different concentrations by agar - well diffusion method. The complex shows enhanced activity against the bacteria and moderate activity against the fungi compared to the free ligands.*

Key words: *Cu(II) complex, 2,4-thiazolidinedione benzoate ion, antimicrobial.*

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I. Introduction

Microwave assisted synthesis, now a days, is an accepted tool for accelerating the organic and inorganic chemical reactions. It leads to high reaction selectivity and consumption of minimum amount of solvents. It is an eco-friendly technique [1,2] and gives a high yield within a very short time. The 2,4-thiazolidinedione (TLD) belongs to a pharmacologically important class of heterocyclic compounds used for the treatment of type-2 diabetes [3-5]. The 2,4-thiazolidinedione and its derivatives lower the plasma glucose levels by acting as ligands for γ-peroxyzome proliferators-activated receptors [6,7]. Besides, this class of heterocyclic compounds possesses various other biological activities such as antihyperglycemic, antimicrobial, anti-inflammatory, anticonvulsant and insecticidal, etc., [8,9]. TLDs are also known for lowering the blood pressure and thereby reducing the chances of heart failure and micro-albuminuria in patients with type-2 diabetes [10,13]. A survey of literature reveals that the metal complexes of many drugs have been found to be more effective than the drug itself [13, 15]. Therefore, much attention is given to the use of TLD owing to its high complexing nature with essential metals.

The present study aims at the synthesis and spectral characterization of Cu(II) complex with 2,4 - thiazolidinedione and benzoate ion ligands. The ligands and their complex are then tested for antibacterial and antifungal activities.

II. Experimental

2.1. MATERIALS AND METHODS

Copper nitrate, 2,4-thiazolidinedione and sodium benzoate were purchased from Alfa Aaser Company and used as such. The organic solvents used, *viz.*, DMSO, DMF, methanol and ethanol were of AnalaR grade and used as such without further purification.

2.2. SYNTHESIS OF METAL COMPLEX

1.0g (8.54 mmol) of 2,4-thiazolidinedione in ethanol and 1.20g (8.20 mmol) of sodium benzoate in ethanol were added to the copper nitrate 1.00g (4.14 mmol) in methanol and followed by microwave irradiation for a few seconds after each addition by using IFB 25 BG-1S model microwave oven. The resulting precipitate was filtered off, washed with 1:1 ethanol: water mixture and dried under vacuum. A blue colored complex was obtained with the yield of 72.0%.

2.3. INSTRUMENTATIONS

CHN elemental analyses were performed using Thermo Finnegan make, Flash EA1112 Series CHNS(O) analyzer. The electrical conductivity measurements were conducted using10^{-3} M solutions of the metal complex in acetonitrile with Systronic Conductivity Bridge (model number-304) at 30°C. The UV-Visible spectrum of the Cu(II) complex was recorded on Varian, Cary 5000 model UV-Vis Spectrophotometer. Infrared spectra for the complex and the ligands were recorded on a Perkin Elmer, Spectrum RX-I, FT-IR Spectrometer in KBr discs at room temperature. The Far-IR Spectrum of the complex was recorded by Bruker 3000, FT- IR Spectrometer. The electron paramagnetic resonance spectrum of the copper complex was recorded at room temperature using JES FA 200 EPR Spectrometer. The antimicrobial and antifungal activities of the ligands 2,4-thiazolidinedione, benzoate ion and their complex were measured by agar- well diffusion method.

2.4. ANTIMICROBIAL ACTIVITY

The free ligands 2,4-thiazolidinedione, sodium benzoate and the synthesized Cu(II) complex were tested for *in vitro* antimicrobial activity by well diffusion method [16], using agar nutrient as medium. The antibacterial and the antifungal activities of the ligands and the Cu(II) complex were evaluated by the well diffusion method against the strains, cultured on potato dextrose agar as medium. In this typical procedure [17], a well was made on the agar medium inoculated with the microorganisms. The well was filled with the test solution using a micropipette and the plate was incubated 24 hours for bacteria and 72 hours for fungi at 35^{o}C. At the end of the period, the inhibition zones formed on the medium were evaluated as millimeters (mm) diameter.

III. Results and Discussion

3.1. Elemental analysis and metal estimation

The elemental analysis and metal estimation of the complex lead to the formula $[Cu(TLD)_4(BEN)_2]$. The percentages of carbon, hydrogen, nitrogen and copper in the complex were found to be 44.41(44.52), 2.88 (2.96), 5.09(5.18) and 11.01(11.70), respectively. The experimental data were in good agreement with the theoretical values.

3.2. Molar conductance

Molar conductance (ΛM) of the complex carried out using acetonitrile as the solvent at the concentration of 10^{-3}M, indicate non-electrolytic [18] behaviour of the complex and conductivity value is found to be $85.8\Omega^{-1}cm^2\,mol^{-1}$. Thus the complex may be formulated as $[Cu(TLD)_4(BEN)_2]$.

3.3. UV-Visible spectrum of Cu(II) complex

The electronic spectrum of Cu(II) complex exhibits three absorbance bands at 680 nm, 343 nm and 280 nm and their corresponding transitions are $^2A_{1g} \leftarrow {}^2B_{1g}$, $^2B_{2g} \leftarrow {}^2B_{1g}$ and $^2E_g \leftarrow {}^2B_{1g}$ respectively, which indicates octahedral geometry around Cu(II) metal ion [19,20]. The magnetic moment value of Cu(II) complex is 1.80 B.M, which is further confirming hexa-coordination around Cu(II) metal ion.

3.4 FT-IR Spectrum

The FT-IR spectra of the free ligands and their Cu (II) complex were recorded in the region of 4000-400 cm^{-1}. The free ligand 2,4-thiazolidinedione exhibited a strong band at 3469 cm^{-1} which could be described as ν(N-H). The peak at 2948 cm^{-1} was assignable to the aliphatic ν(C-H) stretching frequency and ν(C=O) was revealed at 1653 cm^{-1}. The spectra show a peak at 618 cm^{-1} and it may be attributed to C-S-C stretching frequency. On the other hand sodium benzoate shows the frequencies as 1587 cm^{-1} and 1650 cm^{-1} which may be assigned to ν(C=C) and ν(C=O) respectively [21,22]. The aromatic ν(C-H) appears at 3065 cm^{-1}. The IR spectra of the complex is compared to those free ligands 2,4-thiazolidinedione and the sodium benzoate. Upon comparison, the stretching vibrations of the $\nu(NH_2)$ group are observed near 3336 cm^{-1} in Cu(II) complex, lower than those of the corresponding free ligand 2,4-thiazolidinedione. This indicates that the ligand TLD coordinates to the metal via nitrogen atom of the amino group. This trend is in agreement with previous examples of the reported complexes. Then, the ν(C–O), which occurs at 1307 cm^{-1} for the sodium benzoate ligand, is moved to higher frequencies, near 1362 cm^{-1} after complexation. This shift confirms the participation of carboxylic oxygen of the ligand in C–O–M bond formation [23].

3.5 Far IR Spectroscopy

The far-IR spectrum indicates the ligating atom of the ligand linked in to the Cu(II) metal ion of the complex. In the far-IR spectra of Cu(II) complex shows a bands in the region 229-268 cm^{-1} are due to the frequency of ν(M-N) bond [24] of (2,4-thiazolidinedione) in the complex and the frequencies at 484-535cm^{-1} have been assigned to carboxylate oxygen of benzoate ion ν(M-O) mode [25].

3.6. EPR spectrum of copper(II) complex

The spectrum of DMSO solution of Cu(II) complex of 2,4-thiazolidinedione and benzoate ion measured at X-band frequency at 77 K (LNT) provide useful information which is important in studying metal ion environment. The spin Hamiltonian parameters of the complex have been calculated and are summarized in Table 1.

The Cu(II) complex in the frozen state at 77 K shows four well resolved peaks in the low field region and one intense peak in the high field region. The g-tensor value of the copper complex can be used to derive the ground state. In octahedral complexes, the unpaired electron lies in the dx^2-y^2 orbital [26]. For this complex, the observed g-tensor values are $g_{\|}$ =2.2461 > $g_{\perp}$= 2.2103 > g = 2.0023 which suggest that this complex has tetragonally distorted octahedral geometry and the ground state is ^2B_1g. The EPR parameters of the complex coincide well with the related systems which confirm that the complex has an octahedral geometry and it is axially symmetric. In the axial spectra, the g-values are related to the exchange interaction coupling constant G by the expression [27]

$$G = g_{\|} - 2.0023 / g_{\perp} - 2.0023$$

According to Hathaway [28] expression, if G value is larger than four, the exchange interaction is negligible because the local tetragonal axes are aligned parallel or slightly misaligned. If its value is less than four, the exchange interaction is considerable and the local tetragonal axes are misaligned. For the present Cu(II)complex, G is 0.6231, which indicates considerable exchange interaction in the solid complex.

The g_{av} and the covalent in-plane σ-bonding (α^2) parameters are calculated according to the following equation [29]

$$g_{av} = 1/3[g_{\|} + 2g_{\perp}]$$

$$\alpha^2 Cu = (A_{\|} /0.036) + g_{\|} - 2.0023 + 3/7(g_{\perp} - 2.0023) + 0.04$$

Table 1. Spin Hamiltonian parameters of Cu(II) complex of (TLD) **and benzoate ion at 77K**

Complex	**Spin Hamiltonian parameters**					
$[Cu(TLD)_4(BEN)_2]$	$g_{\|}$	$g_{\perp}$	g_{av}	**G**	$A_{\|}$ $10^{-4}cm^{-1}$	α^2
	2.2461	2.2103	0.4321	0.6231	157.62	0.4304

If the α^2 value is 0.4321, it indicates a complete covalent bonding, and if the value is 1.0, it suggests a complete ionic bonding. From Table1, it is clear that the in-plane σ -bonding parameter α^2= 0.4304[30] is less than unity and this indicates the covalent character of M-L bond [31]. These data are well in accordance with the other reported values.

IV. Biological Activity

4.1 Antibacterial activity

The synthesized Cu(II) complex and the free ligands 2,4-thiazolidinedione and sodium benzoate are tested against five bacteria (*staphylococcus aureus, serratia, salmonella typhi, chromobacterium violaceum* and *burkolderia*) at different concentrations (30 µg/ml and 50 µg/ml) by agar-well diffusion method in *vitro* conditions. The complex has moderate activity against the *streptococcus aureus*. On the other hand, the complex has less activity against the (*salmonella typhi)* and does not show any activity against (*serratia, chromobacterium violaceum* and *burkolderia*). The antibacterial activities of the free ligands and the complex are shown in Fig.1

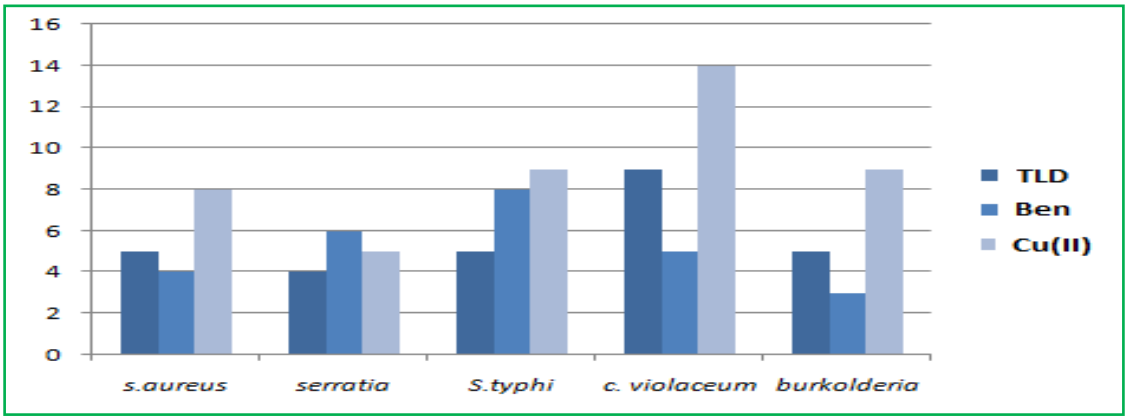

Fig.1 Zone of inhibition (in mm)
Antibacterial activities of the TLD, Benzoate ion and $[Cu(TLD)_4(BEN)_2]$

4.2. Antifungal activity

The antifungal activity of the synthesized Cu(II) complex and the free ligands 2,4-thiazolidinedione and sodium benzoate are assayed using agar -well diffusion method at different concentration (30 and 50 µg/ml). The Cu(II) complex does not show any activity against the fungi (*C.albicance* and *Aspergillus niger*) in both concentration compared to those of 2,4-thiazolidinedione and sodium benzoate ligands.

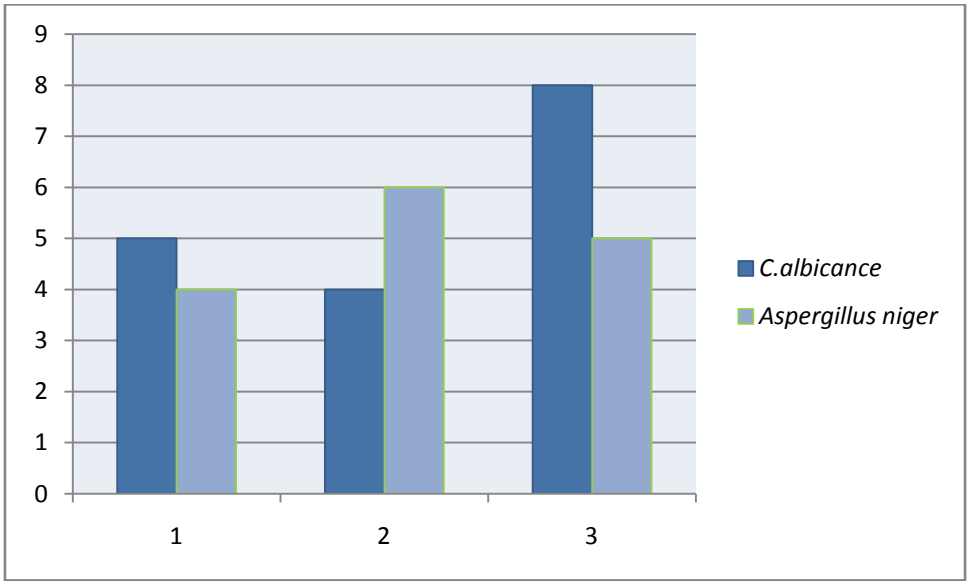

Fig.2 Zone of inhibition (in mm)
Antifungal activities of the TLD, Benzoate ion and $[Cu(TLD)_4(BEN)_2]$

IV. Conclusion

In the present study, our efforts were to synthesize and characterize a new Cu(II) metal complex with 2,4-thiazolidinedione and benzoate ion as ligands. The new complex was synthesized using microwave irradiation. The synthesized compounds were characterized by various chemical and spectral analyses. Based on the analytical, electrical conductance, spectral and magnetic moments data, tetragonally distorted octahedral geometry had been suggested for the Cu(II) complex. The synthesized complex was tested for antimicrobial activities. The Cu(II) complex had significant antimicrobial activities as compared to the free ligands.

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