

PREPARATION, SPECTRAL CHARACTERIZATION AND PHARMACOLOGICAL ACTIVITIES OF TRIVALENT Fe(III) COMPLEX WITH 2,4-THIOZOLIDINEDIONE AND BENZOATE ION AS LIGANDS

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ABSTRACT

A new Fe(III) complex of 2,4-thiozolidinedione and benzoate ion was synthesized using microwave irradiation. The molecular formula and the probable geometry of the complex have been deduced from elemental analysis, molar conductance, UV-Visible, FT-IR and Far-IR spectra. The molar conductance indicates that the Fe(III) complex is a non-electrolyte(1:0) type. The FT-IR spectra show that 2-thiozolidinedione and benzoate ion are coordinated to the metal ion in a monodentate manner. The magnetic moment and UV-Visible spectra indicate that the geometry of the complex is octahedral. The antimicrobial activities of ligands and their Fe(III) complex were studied against the five bacteria (*staphylococcus aureus*, *serratia*, *salmonella typhi*, *chromobacterium violaceum* and *burkholderia*) and also two fungi (*C.albicans* and *Aspergillus Niger*) at different concentrations 30 and 50 µg/ml by agar-well diffusion method. The complex shows significant activity against the bacteria and moderate activity against the fungi compared to the free ligands. The free radical scavenging activity of the complex and the ligands has been determined by measuring their interaction with the stable free radical, DPPH. The complex has larger antioxidant activity as compared to the ligands.

Keywords: Fe(III) complex, 2, 4 thiazolidinedione, benzoate ion, antimicrobial, antioxidant.

1. INTRODUCTION

2,4-thiazolidinedione (TLD) is a pharmacologically very important class of heterocyclic compounds used for the treatment of type-2 diabetes¹. TZD derivatives lower the plasma glucose levels by acting as ligands for γ -peroxylzome proliferators-activated receptors²⁻⁴. In addition, this class of heterocyclic compounds possesses various other biological behavior such as antihyperglycemic, antimicrobial, anti-

inflammatory, anticonvulsant and insecticidal, etc.,⁵⁻⁷. TZDs are also known for lowering the blood pressure and thereby reducing chances of heart failure and micro-albuminuria in patients with type-2 diabetes⁸⁻¹⁰. A survey of literature reveals that metal complexes of many drugs have been found to be more effective than the drug alone¹¹⁻¹³. Therefore much attention is given to the use of TZD due to its high complexing nature with essential metals. On the

other hand, microwave irradiation now a day is an accepted tool for accelerating the organic and inorganic reactions. It leads to high reaction selectivity and utilization of minimum amount of solvents. It is an eco-friendly technique¹⁴⁻¹⁵.

The present study aims at synthesis and spectral characterization of Fe(III) complex with 2,4 - thiazolidinedione and benzoate ion ligands. The ligands and their complex were tested for antibacterial, antifungal and antioxidant activities.

2. EXPERIMENTAL

2.1. MATERIALS AND METHODS

Ferric 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, ethanol were of AnalaR grade, and used as such without further purification.

2.2 SYNTHESIS OF METAL COMPLEX

0.90g(7.47 mmol) of 2,4-thiazolidinedione in ethanol and 1.08g(7.50 mmol) of sodium benzoate in ethanol were added to the Ferric nitrate 1.00g (3.43 mmol) in methanol 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 pale brown colored complex was obtained with the yield: 70.7%.

3. INSTRUMENTATIONS

CHN elemental analyses were performed using Thermo Finnegan make, Flash EA1112 Series CHNS(O) analyzer. The electrical conductivity measurements were conducted using 10^{-3} M solutions of the metal complex in acetonitrile with Systronic Conductivity Bridge (model number-304) at 30°C. 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 antimicrobial and antifungal activities of the ligands 2,4-thiazolidinedione, benzoate ion and their complex was done by agar- well diffusion method.

3.1. Antimicrobial activity

The free ligands 2,4-thiazolidinedione, sodium benzoate and the synthesized Fe(III) complex were tested for *in vitro* antimicrobial activity by

the well diffusion method¹⁶ by using agar nutrient as the medium. The antibacterial and the antifungal activities of the ligands and the Fe(III) complex were evaluated by well diffusion method against the strains, cultured on potato dextrose agar as medium. In typical procedure¹⁷ 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°C. At the end of the period, inhibition zones formed on the medium were evaluated as millimeters (mm) diameter.

3.2. Antioxidant activity

Evaluation of Antioxidant Activity Stock solution (1 mg/ml) was diluted to final concentrations of 10–500 µg/ml. Ethanolic DPPH solution (1 ml, 0.3 mmol) was added to sample solutions in DMSO (3 ml) at different concentrations (10–500 µg/ml)¹⁸. The mixture was shaken vigorously and allowed to stand at room temperature for 30 min. The absorbance was then measured at 517 nm in a UV-Vis Spectrophotometer. The lower absorbance of the reaction mixture indicates higher free radical scavenging activity. Ethanol was used as the solvent and ascorbic acid as the standard. The DPPH radical scavenging activity was calculated using the following equation:

$$\text{Scavenging effect (\%)} = \frac{A_0 - A_1}{A_0}$$

where A_0 is the absorbance of the control reaction and A_1 is the absorbance in the presence of the samples or standards.

4. RESULTS AND DISCUSSION

4.1. Elemental analysis and metal estimation

The elemental analysis and metal estimation of the complex lead to the formula $[\text{Fe}(\text{TLD})_3(\text{BEN})_3]$. The percentages of carbon, hydrogen, nitrogen and metal in the complex were found to be 43.67(44.45), 4.34(4.44), 5.09(5.18) and 10.24(10.34) respectively. The experimental data are in good agreement with the theoretical values (given in the parentheses).

4.2. Molar conductance

Molar conductance measurements of the complex carried out using acetonitrile as the solvent at the concentration of 10^{-3} M, indicate non-electrolyte^[38] behaviour of the complex and conductivity value were found to be

$89.51\Omega^{-1}\text{cm}^2\text{mol}^{-1}$. Thus the complex may be formulated as $[\text{Fe}(\text{TLD})_3(\text{BEN})_3]$.

4.3. Electronic spectra

The iron complexes prepared were red in colour. The ground state term symbol of Fe(III) is ${}^6\text{A}_{1g}$. From the electronic spectrum it is that, the Fe(III) complex exhibit three absorption bands at 680 nm, 385 nm and 260 nm which corresponding transitions can be tentatively assigned ${}^5\text{E}_g \rightarrow {}^5\text{T}_{2g}$, ${}^5\text{B}_{1g} \rightarrow {}^5\text{B}_{2g}$ and CT-band respectively¹⁹ these indicates the six coordinated octahedral geometry. The magnetic moment of Fe(III) complex is 5.09 BM which is further confirmed the hexa coordination around the Fe(III) metal ion.

4.4. FT-IR

The FT-IR spectra of the free ligands and their Fe(III) complex were recorded in the region of $4000\text{--}400\text{ cm}^{-1}$. The free ligand 2,4-thiosolidinedione exhibited a strong band at 3469 cm^{-1} can be assigned as $\nu(\text{N-H})$. The peak at 2948 cm^{-1} assignable to the aliphatic $\nu(\text{C-H})$ stretching frequency and $\nu(\text{C=O})$ revealed at 1653 cm^{-1} . The spectra show a peak at 618 cm^{-1} may be attributed to C-S-C stretching frequency. Then again sodium benzoate shows the frequencies 1587 cm^{-1} and 1650 cm^{-1} may be assigned to $\nu(\text{C=C})$ and $\nu(\text{C=O})$ respectively^{20,21}. The aromatic $\nu(\text{C-H})$ appeared at 3065 cm^{-1} . The IR spectra of the complexes were compared to those free ligands 2,4-thiosolidinedione and sodium benzoate. Upon comparison, the stretching vibrations of the $\nu(\text{NH}_2)$ group were observed near 3324 cm^{-1} in Fe(III) complex, lower than those of corresponding free ligand 2,4-thiosolidinedione. This indicates that the ligand 2,4-

thiosolidinedione coordinate to the metal via nitrogen atom of amino group. The trend is in agreement with previous examples reported complexes. Then, the $\nu(\text{C-O})$, which occur at 1307 cm^{-1} for the sodium benzoate ligand, was moved to higher frequencies, near 1358 cm^{-1} after complexation, this shift confirms the participation of carboxylic oxygen of the ligand in C-O-M bond formation²².

4.5. Far IR Spectra

The Far-IR spectra give the ligating atom of the ligand in to the Fe(III) metal ion of the complex. In the Far-IR spectra of Fe(III) complex shows the new bands in the region $229\text{--}268\text{ cm}^{-1}$ are assigned to the stretching frequency of $\nu(\text{M-N})$ bonds²³ and at $484\text{--}535\text{ cm}^{-1}$ have been assigned to carboxylic oxygen of benzoate ion $\nu(\text{M-O})$ mode²⁴.

5. Biological activity

5.1 Antibacterial activity

The synthesized Fe(III) complex and the ligands 2,4-thiosolidinedione and sodium benzoate were tested against the bacteria (*staphylococcus aureus*, *serratia*, *salmonella typhi* and *chromobacterium violaceum*) at different concentration ($30\text{ }\mu\text{g/ml}$ and $50\text{ }\mu\text{g/ml}$) by agar-well diffusion method in *in vitro* conditions. The complex shows significant 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 *burkholderia*). The antibacterial activities of the free ligands and the complex are shown in Fig. 1.

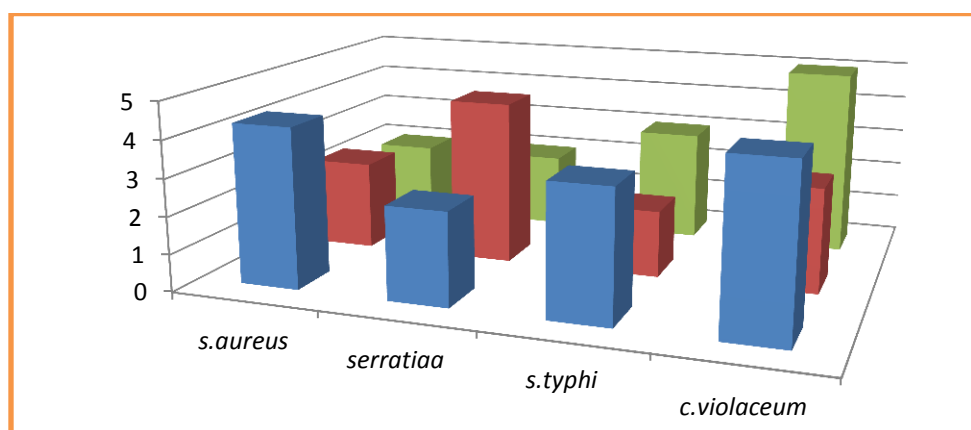


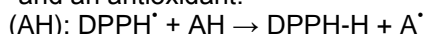
Fig. 1: Zone of inhibition (in mm)
Antibacterial activities of TZD, Benzoate ion and Fe(III) complex

5.2. Antifungal activity

The antifungal activity of the synthesized Fe(III) complex and the ligands 2,4-thiozolidinedione and sodium benzoate were assayed using agar - well diffusion method at different concentration (30 and 50 µg/ml). The Fe(III) complex has does not show any activity against the fungi (*C.albicans* and *Aspergillus niger*) in both concentration compared to that for 2,4-thiozolidinedione and sodium benzoate ligands and copper complex (Fig. 2).

5.3. Antioxidant activity (Radical Scavenging Activity)

The 2,2'-diphenyl-1-picrylhydrazyl (DPPH) radical assay provides an easy and rapid way to evaluate the antiradical activities of antioxidants. Determination of the reaction kinetic types DPPH is a product of the reaction between DPPH• and an antioxidant.



The reversibility of the reaction is evaluated by adding DPPH• at the end of the reaction. If there is an increase in the percentage of remaining DPPH• at the plateau, the reaction is reversible, otherwise it is a complete reaction.

DPPH was used as stable free radical electron accepts or hydrogen radical to become a stable diamagnetic molecule²⁵. DPPH is a stable free radical containing an odd electron in its structure and usually used for detection of the radical scavenging activity in chemical analysis²⁶. The reduction capability of DPPH radicals was determined by decrease in its absorbance at 517 nm induced by antioxidants²⁷. The graph was plotted with percentage scavenging effects on the y-axis and concentration (µg/ml.) on the

x-axis. The scavenging ability of the metal complexes was compared with ascorbic acid as a standard. The metal complexes showed enhance activities as a radical scavenger compared with ascorbic acid, These results were in good agreement with previous metal complexes studies where the ligand has the antioxidant activity and it is expected that the metal moiety will increase its activity²⁸⁻³⁰.

CONCLUSION

In the present study, our efforts were to synthesize and characterize a new Fe(III) metal complex with 2,4-thiozolidinedione 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, octahedral geometry has been suggested for the Fe(III) complex. The synthesized complexes were tested for antimicrobial activities. The Fe(III) complex were significant antimicrobial and antioxidant activities as compared to the free ligands.

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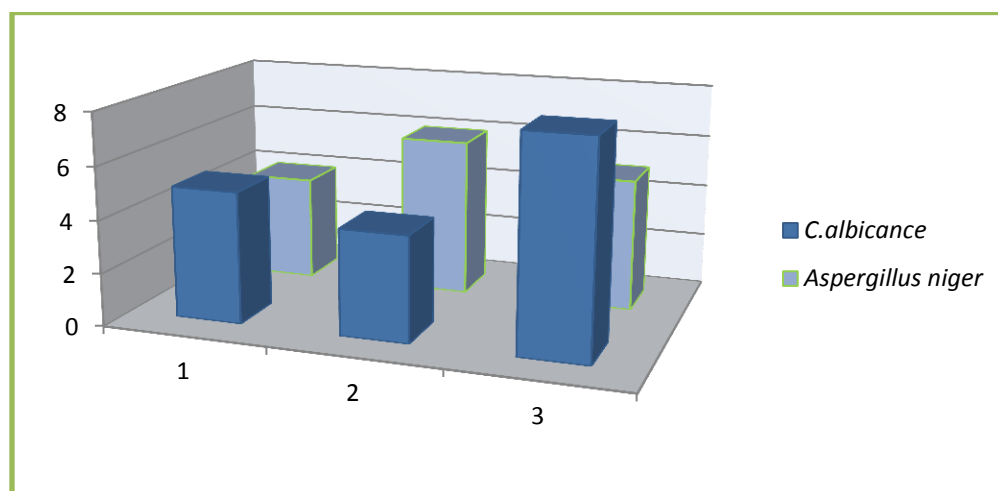


Fig. 2: Zone of inhibition (in mm)
Antifungal activities of TL, Benzoate ion and Fe(III) complex

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