Synthesis and Characterization Zn(II)LeucinDithiocarbamate Complex and Their Potential as Anti-Tuberculosis

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Abstract. Metal-dithiocarbamate complexes find wide-ranging applications in nanomaterial and have potential use as chemotherapeutic and antibacterial. New complexes of Zn(II)LeucineDithiocarbamate have been synthesized using an "in situ" method from reactions of Leucine Dithiocarbamate in mole ratios 1:2 giving the result of around 45,44% and characterized with the instrument of FTIR (Fourier Transform Infra Red), UV-Vis (Ultra Violet Visible), melting point and conductometry. These complex indicate bioactivity more potentials against Mycobacterium tuberculosis as compared to the free ligand with using the LJ method. Therefore, this complex could be used to develop as a new compound in the treatment of tuberculosis

Keywords: *Dithiocarbamate, In Situ Method, Anti-Tuberculosis, Complexes.*

1 Introduction

Tuberculosis (TB) is caused by bacteria (Mycobacterium tuberculosis). Mycobacterium tuberculosis is an infectious bacteria that can attack various organs or tissues of the body1,2. The worldwide mortality rate caused by tuberculosis is increasing3. In 2017, 10 million people fell ill with TB, and 1.6 million died of the disease4. More aggravated by multidrug-resistant TB (MDR-TB) cases which estimate that there are 558,000 new cases with resistance where 82% have MDR-TB5. In order to overcome tuberculosis, many compounds have been synthesized which aim to obtain drugs with higher activity and lower toxicity6.

Some synthetic compounds, such as dithiocarbamate it has been successfully synthesized and shows excellent potential in the field of medicine such as anti-microbial, anti-inflammatory, anticancer and antioxidants7,8,9. Synthesis of dithiocarbamate complexes generally involves the reaction between dithiocarbamate acid and metal in salt form, where dithiocarbamate acid is provided by reacting amines with carbon disulfide in ethanol solvents10.

The aim of this work is to explore the influence of incorporating leucine dithiocarbamate, as a ligand, on the activity of the prepared complexes against tuberculosis bacteria11. Therefore, the synthesis of new drugs with high toxicity and inhibition of M. tuberculosis is needed by using amino acid ligands combined with transition metal ions Zn (II) to study the effects of the presence of various types of ligands on biological activity.

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2 Material and Methods

The materials used in this study were: CS2, ZnCl2, L-Leucine, Test Bacteria (M. tuberculosis), Medium Lowenstein Jensen, ethanol PA, methanol PA, acetone PA, methylene chloride PA, chloroform PA, n-hexane PA, acetonitrile PA, DMSO and KBr

2.1 Synthesis of amino acid dithiocarbamates ligand

To a (0,65gr, 5 mmol) L-Leucine aquabides solution was added dropwise a (0,3 mL, 5 mmol) of CS2 in 10 mL of ethanol, at a temperature below 100C. The solution was allowed to reflux with stirrings for 25 minute.

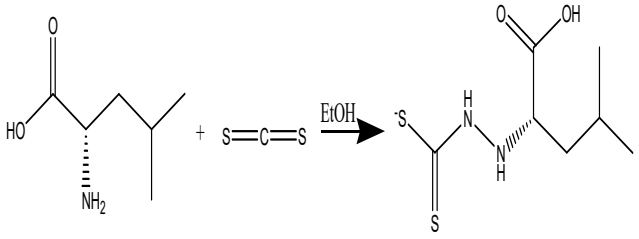

Fig.1. Synthesis reaction of N- Leucin dithiocarbamate ligand

2.2 Synthesis of Zn(II) amino acid dithiocarbamates

A solution of L-Leucindithiocarbamate ligand in ethanol was added to ZnCl2 (0,408 gr; 3 mmol) dissolved in ethanol (10 mL). The solution was allowed to reflux with stirred for 30 minute. The precipitate was then filtered and inserted in the desiccator until dried at room temperature and then crystallized with the appropriate solvent.

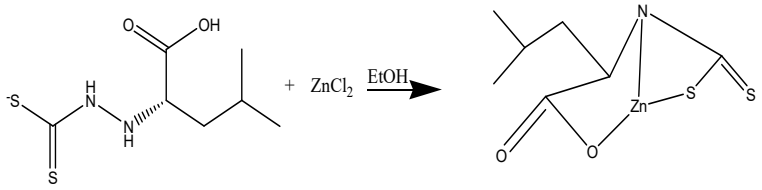

Fig. 2. Synthesis reaction of Zn (II) LeucinDtc

3.3 Characterization

Infrared spectra of the compounds were recorded as KBr discs using Infrared SHIMADZU spectrophotometer, in frequency 4000-300 cm^{-1}. Electronic spectral obtained using UV-Vis Jenwey spectrophotometer 200-1100 nm for 10^{-3}M solutions in ethanolic at 25°C. Melting points were obtained on melting point type WRS-200, and

Conductivity measurements were made with ethanolic solutions using a Eutech Con 510.2 at $25^{o}C$ for complex concentration of 10^{-3} M.

3 Result And Discussion

3.1 Chemical Study

The present our work show that synthesis of complexes and characterization a new Zn(II)leucine dithiocarbamate works successfully (Fig. 2). The ligand was prepared from the reaction of leucin with carbondisulfide in mole ratios 1:2, respectively. The complexes compound was characterised by elemental analysis (Table 1), UV-Vis (Table 2) spectroscopy, and IR (Table 3). The yield of synthesized complexes is 45,44%. The melting point for Zn(II)L-LeucinDithiocarbamate is 338-340 ^{0}C. The conductivity of the synthesized complexes is less than 65 [s/m] which indicates that the complexes are non-electrolytes.

Table 1. Analytical Data for complexes

Compound	Colour	Yield (%)	Melting point (^{0}C)	Molar conductance[S/m]
Zn(II)L-LeucinDtc	white	45.44	338-340	0.163

3.2 UV-Vis Spectroscopy

Dithiocarbamate complexes generally have two main bands. Band I is a transition $\pi \rightarrow \pi^{*}$, band II is a occurs due to the transfer of metal charges to ligands[12,13]. The shift in band I for complexes have been synthesized detected a wavelength between 210-300 nm which is an intraligan transition $\pi \rightarrow \pi^{*}$ of the CS_2 group.The electronic spectra of the Zn(II) complexes shows band 210-300 nm (Table 2, Figure 3) which are assigned to d-d transitions, ligand to metal charge transfer transitions and ligand internal transitions which is bidentate chel. Absorption bands have been assigned to Zn(II) complexes having square pyramidal structure[14].

Table 2. Electronic Spectra For Complexes

Compound	λ (nm)	Electronic transition	log ε
Zn(II)L-LeucinDtc	274	$\pi \rightarrow \pi^{*}$	0,347

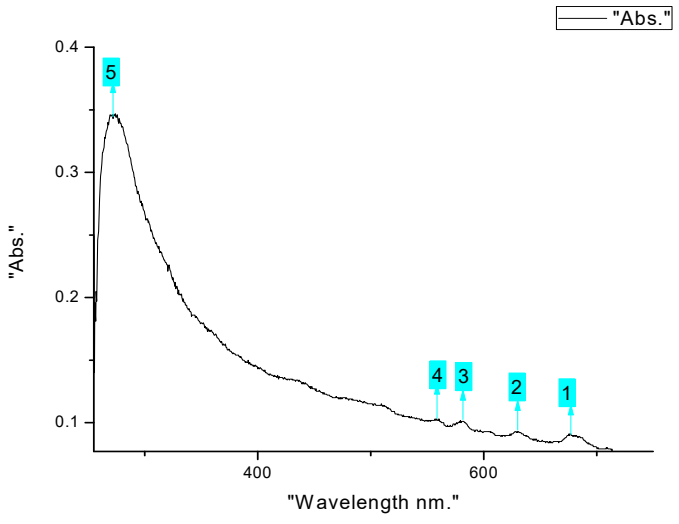

Fig. 3. UV-Vis Spectrum Zn(II)LeucinDtc

3.3 Infrared Spectra

Main of IR spectral vibrations of mixed ligand Zn(II) complexes are given in Table 3. The frequency modes ν(C⋯N) and ν(C⋯S) are diagnostic factors for the dithiocarbamate[15]. The ν(C⋯N) stretching frequency appeared in intermediet between the ν(C-N) in range 1250-1350 cm^{-1} and ν(C=N) in region 1514-1690 cm^{-1}. The (C=N) amine stretching band at 1583,56 cm^{-1} for the complexes compound. That band is assigned to a (C=N) and can be attributed to delocalization of metal electron transition to the $\pi \rightarrow \pi^*$ system of the ligand[11]. The ν(C-S) is written as ν(C⋯S) cm^{-1} stretching frequency appeared in the wave number range 950-1050 cm^{-1} [16]. The ν(M-S) stretching frequency was observed in the range 354-380cm^{-1} [17]. From the data it can be concluded that Zn(II)LeucinDtc has been successfully synthesized and is a bidentate ligand.

Table 3. Selected Infrared Spectral Of The Complexes

Complexes	ν(C⋯N)cm^{-1}	ν(C⋯S) cm^{-1}	V(M-S) cm^{-1}
Zn(II) Leucin Dtc	1583.56	1002.89	364.55

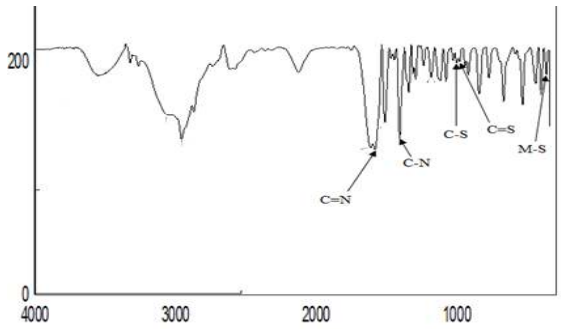

Fig. 4. Infrared spectra of Zn(II)LeucineDtc

3.4 Antimicrobial Study

The ligand macrocyclic and complex compound was reviewed againts *M. Tuberculosis* to assess their potential as an antimicrobial agent by the LJ method at certain concentracion variations. The results of the antituberculosis test are presented in Table 4. The results show that the metal complex is more active than the dithiocarbamate parent ligand for *M. Tuberculosis*. This is caused by the effect of metal chelate Zn (II) which increases lipophilic, from the permeation process through the lipid layer of *M. tuberculosis* cell membranes and can interfere with the integrity of membrane microbial cells resulting in cell damage or cell death characterized by the absence of colony growth in test media LJ[18,19].

Table 4. Population *M. Tuberculosis* For Ligands And Complexes

Compound	Concentration (ppm)	Population M.Tb ligand	Population M.Tb Complex
Zn(II)L-LeucinDtc	0,002	+	-
	0,004	+	-
	0,006	+	-

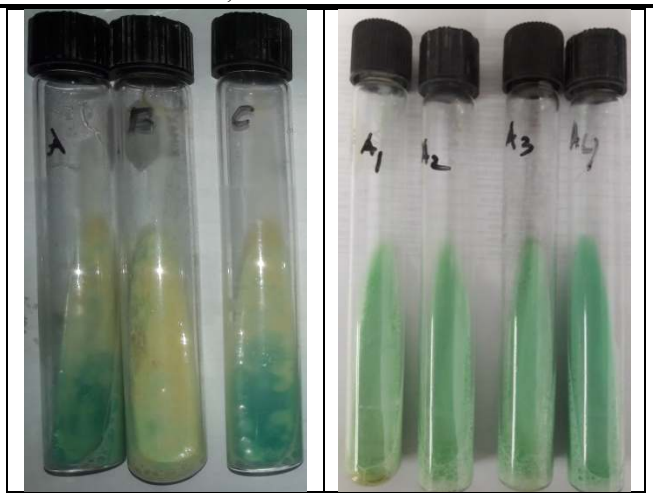

Fig. 5. Antibacterial test result against *M. tuberculosis* A ligand 0,002; B ligand 0,004; C ligand 0,006; A_1 growth controller; A_2 Complexes 0,002; A_3 Complexes 0,004; A_4 Complexes 0,006

4 Conclusion

The Zn(II) Leucindithiocarbamate complexes have been successfully synthesized.The complexes were prepared by addition of metals ion solution in a amino acid leucine and carbon disulfide solution. According of spectral evidences can be known both types of ligands are bidentate.The cytotoxic activity result show synthesized complexes have been more active potential as anti-tuberculosis agents than parent ligands because complex compounds with the addition of metals can increase bacteriostatic activity in *M. Tuberculosis.*

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