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Synthesis, Characterization and Antifungal Activity of Co^{2+} and Ni^{2+} Complexes of N-Ethyl Dithiocarbamate Ligand

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Abstract: *Recently, a lot of papers have reported the fast-rising of microorganisms developing resistance on a drug which is once potent; hence there is a need to embark on the quest for the search of novel antimicrobial material with more specific biological action and good cytotoxicity study. Therefore, more research on metal complex drugs with efficient biological activities will qualify the study on the chemistry of dithiocarbamate complexes. Herein we report a one-pot method of synthesizing complexes of dithiocarbamate using diethyl amine precursor and petroleum ether as the solvent which yielded good amount of product. The characterization and antifungal study of the ligand and complex are also extensively studied.*

Keywords: *Dithiocarbamate, Antifungal, Cytotoxicity, Complexes*

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I. Introduction

Dithiocarbamate fungicides have proved it important in the production of crops; certainly, this is possible due to their high efficiency in eliminating plant fungal diseases and its toxicity level almost negligible. However, more and more studies showed that this kind of fungicides was not easily eliminated and may represent a threat to human health and the environment. Therefore, how to make better use of the advantages of dithiocarbamate-based fungicides and avoid their weaknesses is a problem to be solved. Dithiocarbamates are preferred fungicides for fruits and vegetables due to their strong efficiency and their relatively low human toxicity while being produced quite cheaply.

Cobalt and Nickel, on the other hand, are one of the most important trace elements, present in living organisms in several enzymatic and protein functions. The fungicidal activities of dithiocarbamates based metal complexes are well documented and many dithiocarbamates are commercially available as fungicides, antiviral, antimicrobial. The motivation for the current study, therefore, is to contribute to the recent effort to search for novel antifungal agents from dithiocarbamate copper and zinc complexes.

Herein, we have synthesized a novel Co2+ and Ni2+ complexes of N-ethyl dithiocarbamate ligand with the study of their antifungal assay. Firstly, N-ethyl dithiocarbamate is prepared and characterized. Then the ligand was complex with the trace metals respectively. The experiment indicates the potential utility of such complexes as an antifungal agent.

II. Experimental

2.1. Synthesis of N-ethyl dithiocarbamate ligand

5.8ml of CS_2 was measured and added into a 250ml round bottom flask, 50ml of petroleum ether was added into the same flask which was placed in a water bath to keep the temperature of the system at 0^0C and was allowed to stir for 15mins. 10ml of diethyl amine was added slowly into the already stirring solution which gives a yellow product immediately, the stirring was continuous for 2hours in order to achieve a better yield of the ligand. The yellow product was gotten; the solvent was evaporated using rotary evaporator, 10ml of ethyl-acetate was used to wash the product. Finally, the ligand was dried in desiccators using silica gel as the desiccant.

2.1.1 Synthesis of Bis[N-ethyl dithiocarbamato] Co(II) and Ni(II)

0.13 g of cobalt and 0.184g of nickel salt were weighed and transferred into a 250 ml beaker each. 30 ml of de-ionized water was added into each beaker then stirred to obtain a homogeneous mixture. Also, the calculated mass of the synthesized ligand; (0.166 g x2) was dissolved in 30 ml of de-ionized water each, the solutions were then added respectively and step-wisely into each salt solution. The ligand/metal salt solution mixtures were then stirred vigorously for 2 hours each. A greenish precipitate was obtained for Ni (II) complex,

while a dark blue precipitate for Co (II) complex. Individual reaction products were washed with de-ionized water, suctioned and dried in a desiccator (using calcium chloride as a desiccant). The weights of the synthesized compounds were taken and recorded**.**

2.2 Biological activity

2.2.1 Determination of Zone of Inhibition

Susceptibility of clinically relevant organisms was determined following the Agar Well Diffusion Method for Antimicrobial Susceptibility Testing Version 9.1 (Andrews, 2009). This test is carried out to determine the metal complex compound that will inhibit the growth of the fungi isolate already detected from culturing. The agar well diffusion technique of Willey et al., (2008) was used for the antibiotic sensitivity test. Overnight cultures of the organisms were swabbed on sterile Muller Hilton solidified Agar plates using sterile swab sticks. 30µg of the different metal complex compound was then placed in the agar well. All the plates were incubated at 370C for 24 hours. The zones of inhibition generated by the antibiotics were measured to the nearest millimeters (mm) and interpreted as sensitive (S), Intermediate (I) and resistant (R). The zones of inhibition were measured and interpreted according to (NCCLS, 2000).

The zone of inhibition was determined at the point which an obvious separation between growth and no growth can be seen using a meter rule. Zones of inhibition was measured from the rear of the plate mistreatment mirrored light: the plates were be patient many inches on top of a black echoless surface, and was measured to the nearest millimeter with a meter rule. The zones of inhibition generated by the antibiotics were measured to the nearest millimeters (mm) and interpreted as sensitive (S), Intermediate (I) and resistant (R).

2.2.2 Determination of Minimal Inhibitory Concentration (MIC)

Minimum inhibitory concentration (MIC) was determined by micro-dilution method using serially diluted (6 folds) of the metal complex compound that inhibit the growth of all the bacterial isolates according to the National Committee for Clinical Laboratory Standards (NCCLS, 2000) TMCC. MIC of the metal complex compound was determined by dilution of various concentrations ranging from 10µg/ml, 20µg/ml, 30µg/ml, 40µg/ml, 50 µg/ml and 60µg/ml into six sets of test tubes containing different inoculum respectively. Equal volume of each metal complex compound dilution using micropipette and nutrient broth (9ml) were mixed in a test tube. Specifically, 0.1 ml of standardized inoculum was added in each tube. The tubes were incubated aerobically at 37oC for 18-24 hours. Two management tubes were maintained for every check batch. These enclosed antibiotic management (tube containing extract and growth media while not inoculum) and organism management (tube containing the expansion medium and therefore the inoculum). The lowest concentration (highest dilution) of the metal complex compound that produced no visible bacterial growth (no turbidity) and lowest absorbance as deduced using spectrophotometer when compared with the control tubes were regarded as MIC.However, the MBC was determined by sub-culturing the test dilution on to a fresh drug free solidified nutrient agar medium and incubated further for 18-24 hours. The highest dilution that yielded no signal bacterial colonyontheculturemediumwastakenasMBC.

III. Indentations and equations

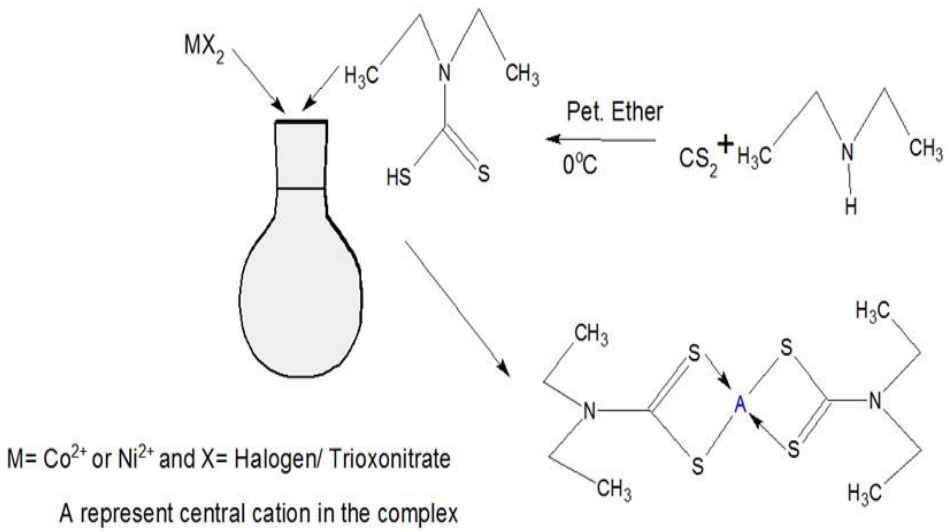

Fig 1: Reaction Scheme

IV. Figures and tables

Table 4.1: Solubility test result

Solvent Reagent	[L DTC]	[Ni $(L)_2$]	[Co $(L)_2$]
Methanol	Slightly soluble	Soluble	Slightly soluble
Ethanol	Slightly soluble	Slightly soluble	Slightly soluble
Hexane	Sparingly soluble	Not soluble	Slightly soluble
Toluene	Very soluble	Soluble	Slightly soluble
DMSO	Soluble	Soluble	Very soluble
Chloroform	Very soluble	Soluble	Very soluble
Diethylether	Soluble	Slightly soluble	Not soluble
Xylene	Very soluble	Soluble	Slightly soluble

Key:
[L DTC] = N-ethyl dithiocarbamate ligand
$Co[L]_2$ = Bis[N-ethyl dithiocarbamato] cobalt (II) ion
$Ni[L]_2$ = Bis[N-ethyl dithiocarbamato] cobalt (II) ion

Table 4.1.2: Summary of the melting point and yield percentage for both the ligand and their respective metal complexes

Ligand/metal complexes	Melting point	Yield percentage
$Co[L]_2$	225^0C	75%
$Ni[L]_2$	247^0C	60%
[L DTC]	201^0C	70%

Table 4.1.3: UV-Visible Electronic Spectra

S/N	COMPOUND	λ_{max} (nm)
1.	[L DTC]	355.0
		279.5
2.	$Co[L]_2$	278.0
		355.0
3.	$Ni[L]_2$	282.0
		378.5
		590.0

Table 4.1.4: FTIR Spectra data

S/N	COMPOUND	V(C-N)cm^{-1}	V(C-S)cm^{-1}	V(N-H)cm^{-1}
1	[L DTC]	1458	984	-
2	$[Co(L)_2]$	1502	1004	-
3	$[Ni(L)_2]$	1520	992	-

4.1.5 In-vitro Antimicrobial Studies

The antifungi studies of the free ligands and their metal complexes were recorded in dimethyl sulphoxide against six fungi isolates, using agar well dilution method. The data for the zones of inhibition recorded by the synthesized compounds against the pathogens of interest are contained in Table 3.1.5. DMSO was used as an internal reference and mycotine as the commercial antifungi agent. The minimum inhibitory concentration was done within the range of 5.0-30.0 µg/ml.

Test organism	[L DTC]	$[Ni(L)_2]$	$[Co(L)_2]$	DMSO	MYCOTIN
Rhyzopus	23	20	25	14	24
Aspergillus flavus	22	26	0.0	0.0	23
Alternaria	36	32	33	26	34
Aspergillus niger	24	34	36	16	0.0
Yeast	27	30	25	0.0	23
Candida	0.0	14	17	0.0	12

Key: Sensitive: 26nm and above; intermediate (i) = 21-25 nm; resistance (r) = 0-20nm

4.1.6 Result of the antimicrobial assay showing the zones of minimum inhibitory concentration of metal complex on fungi

The MIC study was done at a range of 5 to 30 µl. Most of the metal complex and ligand did not show visible sensitivity at some of the pathogen within the minimum concentration, but for Nickel (II) complex it shows sensitivity at 5 µl each on Fusarium, Aspergillus flavus, Alternaria and Aspergillus niger. The result also showed that the ligand and both metal complexes are active against Alternaria at 5 µl each.

V. Discussion

5.1 Solubility

The solubility results recorded for the ligands and their metal complexes showed that while the ligands were both soluble in water as well organic solvents (Table 4.1); their metal complexes were only soluble in DMSO, toluene, diethyl ether, and chloroform while they were not soluble in methanol, ethanol, and xylene. This finding suggests that the metal complexes are non-polar.

5.1.1 Melting Point

The metal complexes melting point was recorded using the electrothermal digital melting point with a capillary tube, and the values were found to range between (197-258)¬¬¬0C. The result showed that the ligand and their metal complexes were stable in a solid-state at room temperature above 2010C and below 2470C.

5.1.2 Electronic Spectra Studies

Ekennia and Odola (2013) and Fouad et al., (2010) have reported that bands on the UV-visible spectra around (333-256nm) are assigned to intra-ligand ( ) transition and the weak absorption at (650-490nm) is attributed to d-d transition; while Fouad et al, (2010) publication assigned ligand metal charge transfer (LMCT) transition to bands around (454-345nm). Also, Adii et al., (2013) attributed the absorptions recorded in the UV-visible spectra of their metal complexes in the region 800nm as due to intramolecular transition in dithiocarbamate ligand containing the involvement of the NCS2 moiety in all their metal complexes.

In these present studies, all the metal complexes showed absorption at (355nm) suggesting that NCS2 moiety was involved in the complexation of the metal ions with ligand [Ejelonu et al., 2016; Yiase et al., 2014;]. The complex gave an absorption at (590nm) in the UV-visible spectral which can be assigned to d-d transition; which also showed that the complex geometry is sphere planar [Ekennia and Odola., 2013; Ajibade et al., 2015], while the 282.0nm absorption could be assigned to ligand metal charge transfer (LMCT).

The 279.5nm observed in the UV-vis spectrum could be assigned to transition – Intra ligand transition in the L-L metal complex. Nickel complex at 567nm showed a weak absorption attributable to the d-d transition (1A1g- 1A2g) supporting a square planar geometry for nickel complex. [Ekennia and Odola, 2013], [Ejelonu and Ajibade, 2016].

5.1.3 FTIR Studies

The ligands, as well as the two metal complexes prepared, showed the characteristics absorption bands often associated with DTC; The v(C-N) stretching vibration in the region 1580-1450 cm-1 and the v(C-S) absorptions in the region 1060-940 cm-1 [Ajibade et al.,2012; Kumar et al., 2011]. The v(C-N) absorption observed in the ligand (L) 1458 cm-1 shifted to a higher wavenumber in all the metal complexes formed between (1060-940) cm-1. The shift to higher wavenumber in the v(C-N) bands in the two metal complexes is in good agreement with other published work [Onwidiwe and Ajibade, 2011; Hamdi and Mustapha,2013; Ajibade & Ejelonu, 2013]. The v(C-S) stretching vibration of the NCS2 group was observed in the region (992-1004) cm-1 for the two metal complexes and 984 cm-1 for the dithiocarbamate ligand. The v(C-S) data also showed an increase in wavenumber of the metal complexes relative to the ligand. The presence of v(C-N) and v(C-S) stretching bands confirmed the presence of dithiocarbamate ligand in the synthesized complexes [Ejelonu & Ajibade., 2016; Khan et al., 2011; Nahipour et al.,2013 and for more references see Ejelonu and Ajibade references Number 41]. The (N-H) stretching band was absent in both ligands and the metal complexes as the ligands were synthesized from a secondary amine. The Asymmetric alkyl group stretching was observed at 2980 cm-1 for the free ligand, and at (2980-2986) cm-1 for the Cobalt (II) and Nickel (II).

5.1.4 Antimicrobial Studies

The result showed that Nickel complex showed improved antifungal potency against Aspergillus niger, Candida, Yeast, Rhizopus, and Aspergilliusflavus respectively, this observation was supported by the works of [Kamal et al.,2005; Yiase et al.,2014, Ajibade et al., 2012, Mikkat et al., 2013, Jassim et al.,2012].

This observed resistance to the pathogenic species may be attributed to the low permeability of the metal complexes through the fungi cell wall. This finding is in agreement with the work of [Ekennia et al., 2015]. The Nickel complex with a zone of inhibition value of (30mm) over that of mycotin (12mm) could serve as a better antifungal agent over mycotin if further studies are carried out on it. At the experimental

concentration of 25µg/ml, the synthesized ligand and it's metal complex showed good in-vitro anti-fungi inhibitory properties (table 4.1.5).

The metal complexes show improved anti-fungi potency compare to uncomplexed ligands against most of the tested organisms. This is in good agreement with some published studies on metal complexes and their anti-fungi properties against Mucor, Yeast, and Candida.

At the experimental concentration, the ligand recorded a good inhibition zone value of 5mm against Alternaria and Aspergillus niger.

VI. Conclusion

The study of inorganic chemistry has contribution immensely to pharmacy. A lot of new discoveries to initiate new methods for procedural synthesis of various metal complexes and dithiocarbamate ligands and this has brought hope to us as research is still ongoing over the use of these potent drugs. From the findings of this study it was shown that:

- Diethyl dithiocarbamate could serve as a useful drug against many pathogens causing diseases.
- The melting point of the metal complexes ranged from (201-247)^{o}C
- The metal complexes are insoluble in water but are majorly soluble in non polar organic solvents
- The activities of the synthesized complexes against the selected pathogens varied between the complexes and the pathogens. The complexes showed reasonable activities against some of the selected pathogens while some of the pathogens were resistant.

The metal complex of cobalt and nickel have antifungal activity, hence, it can be used as an antibiotics towards Alternaria, Aspergillus nigera and Mucor. Therefore, it may be recommended that the subsequent studies of the metal complexes on the pathogens should be carried out at higher concentrations

Since there is a lot of needs in the pharceutical world to provide cure to so many diseases both existing and new ones there is need to embark on further study to know the proper applications of the synthesized drugs to the selected pathogens. Therefore, the synthesized ligands and their metal complexes could be compounded into modern drugs.

However, there may be need to carry out further research on the said compounds to ascertain their safety and dose dependence. This should enforce a collaborative effort between the chemists and pharmacists in our various research institutes and Universities in discovering the use of these complexes and ligands.

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References

[1]. Ajibade, P. A.; Kolawale, G. A. Synthesis, Characterization and Antimicrobial studies of Metal Complexes of Sulfadiazine with N-Alkyl-N-Phenyl Dithiocarbamate. Bull. Chem. Soc., 2008, 22 ,261.
[2]. Ajibade, P.A.; Ejelonu, B.C. Group 12 dithiocarbamates complexes; synthesis, spectra studies and their uses as precursors for metal sulphide nanoparticles and nanocomposites. Spectrochim Acta A mol Biomol Spectroscopy., 2013, 408-414.
[3]. Anthony, C. E. Antibacterial Application of Novel Mixed-Ligand Dithiocarbamate Complexes of Ni(II). (IOSR-JAC), 2013, 5(2): 36- 39.
[4]. Anthony, C. E.; Odola, A.J. Synthesis, physic-chemical Charcterization and Biocidal studies of Ni(II) mixed ligand complexes of Alkyl Dithiocarbamate and Salicyaldehyde. Int. J. Phar. Biol and Chem Sci., 2013, 2(3): 21-25.
[5]. Ejelonu, B.C.; Synthesis, Characterization of Mixed N-phenyl-p-chlorophenyl Dithiocarbamate ligand complexes of some transition metals and their in-vitro antimicrobial activities. Wikipedia 2015
[6]. Dhanalaskshmi M. Synthesis, Characterization and Antimicrobial Activity of Some Mixed Ligand Metal Complexes. Department of chemistry, SFR College for women, Sivakasi, Taminadu, India. 2013, vol. 2(6): 109-119
[7]. Ejelonu, B.C. Synthesis, Characterization of Mixed N-phenyl-p-chlorophenyl Dithiocarbamate ligand complexes of some transition metals and their in-vitro antimicrobial activities. EJBPS, 2016, 3(10): 33-37.
[8]. Anthony. E. C and Odola A. J. and Anthony J.; Synthesis, physic-chemical characterization and biocidal studies of nickel (ii) mixed ligand complexes of alkyl dithiocarbamate and salicyladehyde. International journal of pharmaceutical, biological and chemical sciences, 2013, accepted manuscript I.d; 2040837151
[9]. Leka Z.B, Leovac V.M, S.R Likic S, Sabo T.J, Trifunovic and Katalin M.S. Synthesis and physic- chemical characterization of new dithiocarbamato ligand and its complexes with copper(II), nickel (II) and palladium(II). J. Therm Anal and Cal. 2006, 83
[10]. Leka, Z.B; Leovac, V.M; Likic, S.; Sabo T.J; Katalin, M. Synthesis and physic- chemical characterization of new dithiocarbamato ligand and its complexes with copper(II), nickel (II) and palladium(II). J. Therm Anal and Cal. 2006, 83.
[11]. Manohar A, Ramalingam K, Thiruneelakandan R, Boceli G and Righi L. N-(2- hydroxyethyl)-N-methyldithiocarbamato complexes of nickel(II) with phosphorus donor ligangs. AnorgAllg.Chem. 2006, 632:461-464.
[12]. Mcelwa Mamba Saul, Electronic data UV- vis spectra 2010 pg. 53
[13]. Shaker, S.A; Mohammed, H.A; Salih, A.A. Preparation, Pysio-chemical and Spectroscopic Investigation of Thiacetazone Quinalizorine complexes with Mn(II), Fe(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Pd(II). Aus. J. Basic Applied Sci., 2010, 10, 5178-5183
[14]. Raghad, Haddad, springer plus, Electronic Spectroscopy UV-vis spectra 2013 pp. 2.5 and 10.
[15]. Yiase S.G, S.O. Adejo, J.A. Gbertyo and J Edeh., synthesis, characterization and antimicrobial studies of salicyclic Acid Complexes of some Transition Metals, Journal of Applied Chemistry (IOSR-JAC)

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