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Synthesis, Characterization and Antimicrobial Studies of Terpene Derived Ligand and Its Metal(II) Complexes

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Abstract: Terpene-derived ligand from (2,4-dinitrophenyl)hydrazine and camphor and its Cu(II) and Fe(II) complexes were synthesized and characterized by melting point and decomposition temperature, elemental analysis, molar conductivity, infrared (IR) spectral analysis, solubility test and magnetic susceptibility. The structures of Cu(II) and Fe(II) with terpenoid ligand have been composed from reacting between copper bromide and iron bromide with hydrazone in 1:2 molar ratio. The ligand and its metal complexes have been detached in a solid state. The spectroscopic data of the structures proposes their 1:2 structures which are characterizedby CHN, FT-IR and From spectroscopic reviews we proposed the octahedral structure for the all structures and the outcomes are spoken to and talked about underneath. The antibacterial and antifungal activities of the ligand and metal(II) complexes were evaluated by applying disc diffusion method. The antibacterial assay was carried out on four pathogenic bacteria, *Escherichia coli*, *Proteus aureginosa*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, and three fungi, *Candida albicans*, *Candida utilis* and *Saccharomyces cerevisiae*. The ligand and its metal(II) compounds showed some antibacterial and antifungal activities but having lower activity when compared to the control drugs.

Keywords: Metal(II) complexes, terpene-derived ligand, camphor, (2,4-dinitrophenyl)hydrazine.

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1.0 INTRODUCTION

These days, metal complexes are employed extensively in medicine for disease management, diagnosis, and treatment. For example, Cu(II), Co(II), Zn(II), and Fe(II) complexes formed from acetaminophen and acetylsalicylic ligands had biological activity against *Escherichia coli* and *Staphylococcus aureus*. Additionally, high-inhibitory efficacy against Candida strains is demonstrated by Cu(II) and Ni(II) metal complexes generated from dihydropyrazole ligands (Mohammed and Tripathi, 2020).

The medicinal applications of camphor have been recognized since ancient times, it has a very long history of traditional applications. Pharmacological uses of camphor include liniments and balms for relief of muscular pain, inhalants for nasal decongestion, antitussives, and expectorants. The activity of camphor on nasal decongesting was attributed to the stimulation of cold receptors in the nose. Such behavior triggered our interest in the ability of camphor derivatives, in particular camphor derived complexes, to interact with other biological targets and also to evaluate their antimicrobial properties [Görnemann, *et al.*, 2008; Al-Saadawy, 2016 and Costa, *et al.*, 2021).

One of the most potent and effective contributions of contemporary science and technology to the management of infectious diseases is the discovery and development of antibiotics. Synthetic chemists are motivated by this to look for novel metal complexes of bioactive substances. The coordinating domain Because of its uses and significance in the field, chemistry is developing quite quickly. Numerous Schiff base ligands and associated metal complexes have been created, studied, and assessed for their potential biological applications (Jabbi *et al.*, 2020).

The biological implementations and chelating ability of metal complexes have attracted significant concern. Transition metal(II) complexes have been widely investigated due to their various biological applications in pharmacological fields. These complexes were reported to have antitumor, anti-inflammatory, antioxidant, antimalarial, and antimicrobial

activities [Qin, *et l*., 2013 and Wang, *et al*., 2012]. Metal complexes with N, O as their donor atoms are very noticeable because of their important biological activities like anticancer, and herbicidal activity. In this study the ligand was synthesized and its divalent metal(II) complexes were prepared. Eventually, the ligand and its complexes were then characterized and their antibacterial and antifungal activities were also ascertained.

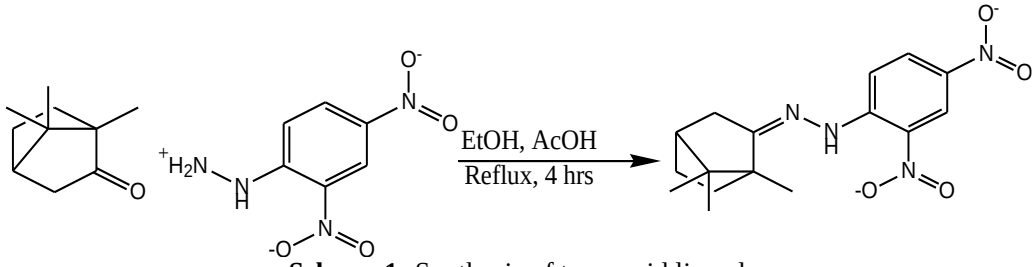
2.0 MATERIAL AND METHODS

2.1 Chemicals, Reagents and Apparatus

All the reagents used in this research work were of analytical grade and used without further purification. All weighing was carried out using an electric balance model AB54. The IR spectral analysis was recorded using Cary 630 FTIR Agilent Technologies. Conductivity measurements were carried out in DMSO solvent employing Jenway 4010. Melting point and decomposition temperature measurements were obtained with a SMP10 STUART melting point apparatus. The *in vitro* antimicrobial screening was performed by using disc diffusion method.

2.2 Synthesis of the Terpene-derived Ligand

(2,4-dinitrophenyl) hydrazine (0.01 mol) was added to camphor (0.01 mol) in ethanol (25 mL).The subsequent solution was refluxed on a water bath for 4 - 5 hours. Also 2 – 3 drops of acetic acid was added to the reaction mixture, then poured onto a measuring glass containing an ice/water blend. The resultant precipitate was separated by filtration, washed with ethanol and diethilether and dried to give orange gems. Yield: 88 %, m.p. 189 °C (Alsaadawy 2011).



Scheme 1: Synthesis of terpenoid ligand

2.3 Synthesis of the metal (II) Terpenoid Complexes

To the hot solution of (0.001mol) terpenoid ligand in (35cm^3) ethanol, a hot ethanolic solution of (0.001mol) metal(II) chlorides was added in mole ratio 1:2 in ethanol (20cm^3). The subsequent solution was refluxed on a water bath for 4 - 5 hours Also 2 – 3 drops of acetic acid was added to the reaction mixture. The mixture was cooled at room temperature and the complex was precipitated and dried.

2.4 Physical measurements

The IR spectroscopy of the ligand and its metal(II) complexes were recorded employing FTIR Carry Agilent 630 spectrophotometer at 4000 - 650 cm^{-1} region in KBr pellets. C, H and N were estimated employing elemental analyzer Perkin-Elmer model 240c. Jenway 4010 conductivity meter was used in conductivity measurement using DMSO as solvent. Melting point and decomposition temperature were obtained by using SMP10 STUART melting point apparatus. The magnetic susceptibility of the complex was measured on Gouy's balance at room temperature.

2.5 Antibacterial and Antifungal Test

The method used by Jorgensen [Jorgensen, and Turnidge, 2003] was used in antibacterial test, in which the ligand and its metal(II) complexes were assayed employing ager disc diffusion method using cultures of *Escherichia coli, salmonella typhi and staphylococcus aureus*. The samples were separately dissolved in dimethylsulfoxide to have three different concentrations (1000, 2000 and 3000) µg/disc. Each of these was separately put on top of the culture media before incubation for 24 hrs at 37°C. Also the diameter of inhibition zone produced by the ligand and its metal(II) complexes were taken and recorded. Similar procedure was applied in antifungal by using *Aspergillus flarus, Aspergillus niger* and *Mucor indicus* fungal isolates.

3.0 RESULTS AND DISCUSSION

3.1. Physical Properties of the Ligand and its Metal(II) Complexes

The ligand and its metal(II) complexes were prepared in good yield, the physical properties of the synthesized ligand and its complexes were analyzed and presented in table 1. The percentage yield of the ligand was 88 % while that of the complexes were 79 and 77 %. The ligand was orange whereas the Cu(II), and Fe(II) complexes were brown respectively. It was found that the melting point of the ligand was 189^{O}C and the decomposition temperature of the metal(II) complexes were 182 and 153^{O}C, this is an indication of their thermal stability.

Table 1: Physical Properties of the Ligand and its Metal(II) Complexes

Compounds	Colour	% yield	M.P. (^{O}C)	D. Temp (^{O}C)
L (Ligand)	Yellow	88	189	-
$[CuL_2(H_2O)_2]$	Brown	79	-	182
$[FeL_2(H_2O)_2]$	Brown	77	-	153

Keys: M.P = Melting Point, D. Temp. = Decomposition temperature

3.2 Solubility Test

Some common organic solvents and water were used to ascertain the solubility of the ligand and its metal(II) complexes. Also from the result of solubility test presented in table 2, the ligand and its metal(II) complexes were found to be soluble in dimethylsulfoxide and dimethylformamide, insoluble in n-hexane and water and slightly soluble in methanol.

Table 2: Solubility test of the Ligand and its metal(II) complexes

Compound			Solvents			
	Acetone	CCl_4	DMF	DMSO	Methanol	water
L (Ligand)	SS	S	S	S	SS	IS
$[CuL_2(H_2O)_2]$	SS	SS	S	S	SS	IS
$[FeL_2(H_2O)_2]$	SS	SS	S	S	SS	IS

Keys: S = Soluble, SS = Slightly Soluble, and IS = Insoluble

3.3 Elemental Analysis

The elemental analysis values of the ligand and its metal(II) complexes for C, N and H determined, indicated that the stoichiometry of all the complexes are 1:2 (metal to ligand ratio) and recorded in Table 3. Also, the elemental analysis details of the ligand suggested the formation of the ligand while that of the complexes revealed the formation of $[CuL_2(H_2O)_2]$ and $[FeL_2(H_2O)_2]$. This is inconsistent with Jabbi's work [Jabbi, *et al*., 2020].

Table 3: Elemental Analysis Data of the and its Metal(II) Complexes

Compound		Found /(Calculated) %	
	% N	% C	% H
L (Ligand)	16.86 (16.47)	64.39	6.07 (6.03)
$[CuL_2(H_2O)_2]$	14.70 (14.74)	50.42 (50.34)	5.55 (5.48)
$[FeL_2(H_2O)_2]$	14.85 (14.46)	50.94 (50.76)	5.61 (5.45)

3.4 FTIR Analysis

The infrared spectral analysis of the ligand and its metal(II) complexes were determined. The band observed at 1389cm^{-1} in the ligand is attributed to *v*(NO), and it shifted to 1332 and 1336cm^{-1} in the complexes, which indicate the participation of nitro oxygen atom in bonding with the respective metal(II) ions. The broad band at 3086, 3088 and 3088cm^{-1} in ligand and the complexes spectra are assigned to (C-H) Ar stretching vibration. The FTIR spectral details of the ligand determined displayed a band at 1641cm^{-1} and it was attributed to *v*(C=N), a feature of azomethine group. The same band was observed to shift to lower frequencies 1612 and 1610cm^{-1} in the complexes suggesting coordination of the ligand to the respective metal(II) ions [Mounika, *et al*., 2010; Rasha, S and Farah, 2012]. New bands in the metal(II) complexes appeared at 464 and 482cm^{-1} and 505 and 518cm^{-1}they are assigned to *v*(M-N) and *v*(M-O), stretching frequencies respectively (Table 4).

Table 4: Infrared spectral data of the Ligand and its metal(II) complexes

Compound	*v*(N-O) (cm^{-1})	*v*(C-H)Ar (cm^{-1})	*v*C=N (cm^{-1})	*v*M-N (cm^{-1})	*v*M-O (cm^{-1})
L (Ligand)	1389	3086	1641	-	-
$[CL_2(H_2O)_2]$	1332	3088	1612	464	505
$[FeL_2(H_2O)_2]$	1336	3088	1610	482	518

3.5 Antimicrobial and antifungal Activity

The antimicrobial actvity results of the screened ligand and its metal(II) complexes were given in the table 5. The ligand and its complexes were screened for their antibacterial activities against the selected bacteria isolates of *Eschirichia coli*, *Salmonella typhi* and *Staphylococcus aureus*, by disc diffusion method. It was discovered that the metal(II) complexes possess more effect in inhibiting the microbial growth. This is possibly because of the interaction of the metal(II) complexes with lipoproteins of the cell. Therefore the metal(II) complexes can restrict the usual functioning of the microbial cell. Furthermore, higher stability of the complexes at higher temperature can also allow them to be used as a

potential antimicrobial agent. Similar result was also recorded in table 6 for antifungal activity shown by selected fungi isolates of *Aspergillus flarus, Asphergillus niger and Mucor iudicus* respectively.

Table 5: Antibacterial activity of the Ligand and its metal(II) complexes

Compound	Concentration (μgcm^{-3})	Bacterial inhibition zones in mm		
		Staphylococcus aureus	Eschirichia coli	Salmonella typhi
L (Ligand)	1000	09	09	09
	2000	06	08	10
	3000	07	09	08
$[MnL(H_2O)_3].H_2O$	1000	09	10	10
	2000	11	13	12
	3000	13	18	15
$[FeL(H_2O)_3].H_2O$	1000	12	11	11
	2000	11	16	14
	3000	15	17	14

Table 6: Antifungal activity on the Ligand and its metal(II) complexes

Compound	Concentration (μgcm^{-3})	Fungal inhibition zones (mm)		
		Aspergillus Flarus	Mucor Iudicus	Asphergillus Niger
L (Ligand)	1000	06	03	04
	2000	08	05	06
	3000	09	07	07
$[MnL(H_2O)_3].H_2O$	1000	10	11	12
	2000	12	16	15
	3000	20	20	19
$[FeL(H_2O)_3].H_2O$	1000	11	09	11
	2000	15	12	14
	3000	18	17	17

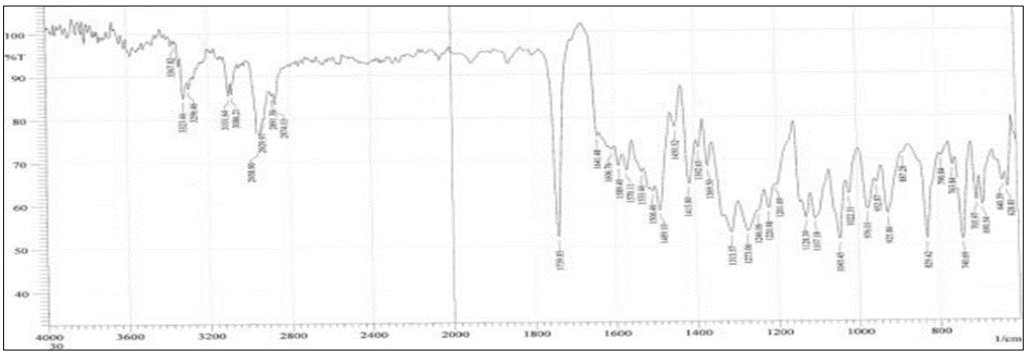


Figure 1: FTIR of Ligand

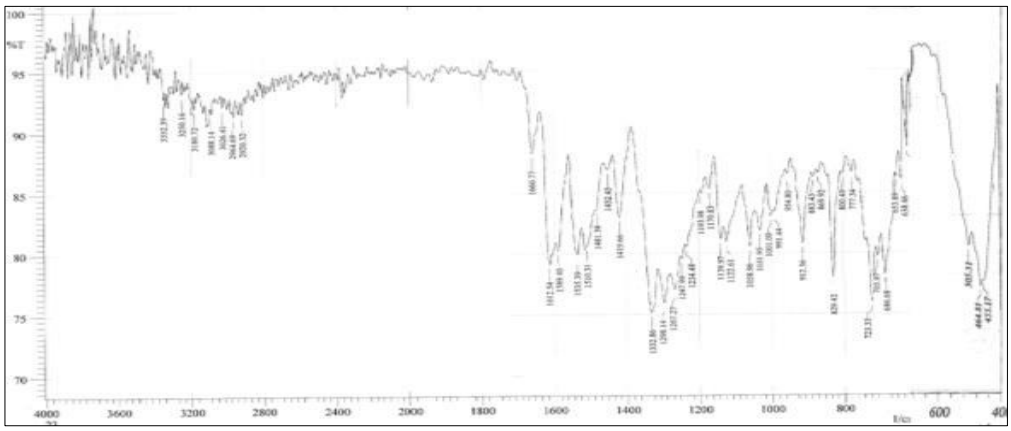


Figure 2: FTIR of Cu(II) complex

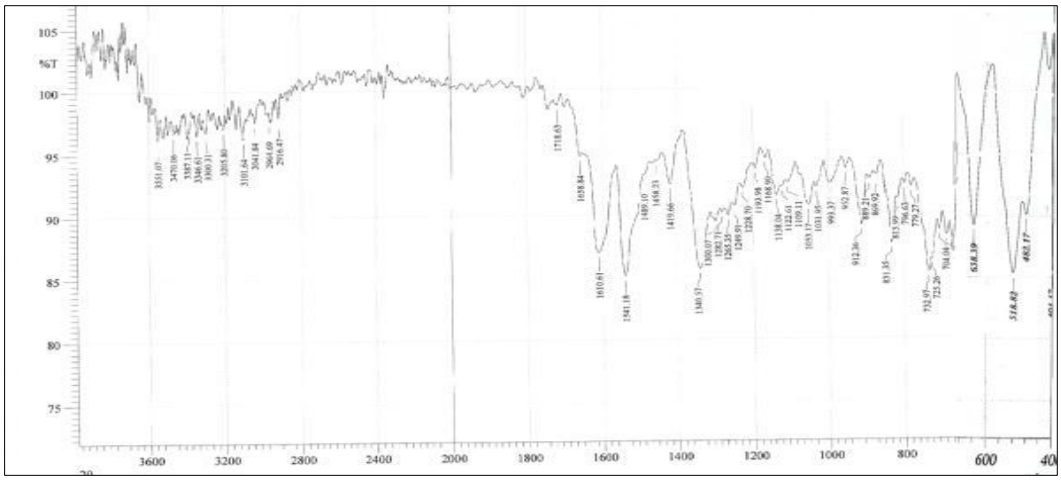


Figure 3: FTIR of Fe(II) complex

4.0 CONCLUSION

The ligand and its metal(II) complexes were synthesized and characterized. The molar conductance values of the metal(II) complexes obtained were low, this indicated the non electrolytic behavior of the complexes. The elemental analysis data suggested 1:2 metal to ligand ratio. The IR data indicated that the ligand was coordinated to the central metal(II) ion in a tridentate manner via the azomethine nitrogen and phenolic oxygen atoms after deprotonation. The result of the solubility tests showed that the ligand and both of its metal(II) complexes were soluble in dimethylsulphoxide (DMSO) and dimethylformamide (DMF), slightly soluble in acetone and ethanol and insoluble in water. The ligand and its complexes were also screened for their antimicrobial activities against three selected fungi and bacteria isolates using disc diffusion method respectively. The complexes were found to be more active than the ligand but less than the reference drugs *Amoxicillin* and *Ketoconazole* used respectively.

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