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A novel Copper (II) Schiff base complex: Synthesis, characterization and antibacterial activity

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ABSTRACT

The current study focuses on synthesis, characterization and antimicrobial activity of cu (II) with N-(3-nitrobenzylidene)-4-cholorobenzenamine Schiff base ligand. Coordination compound for cu (II) with N-(3n nitro benzylidene)-4-cholorobenzenamine Schiff base ligand was derived from 3 nitro benzaldehyde an para choloro aniline Ligand and its copper complex were characterized using FT-IR, HNMR and CNMR spectra. Finally, the antimicrobial effect of the complex on *E. coli* was investigated by minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) tests. FT-IR, HNMR and CNMR spectra showed the success of production new complex. Minimum inhibitory concentration and minimum bactericidal concentration studies showed the enhanced antibacterial effect of new complex on *E.coli*. The results showed that new complex has numerous antimicrobial effect on *E.coli*.

Introduction

Transition metal complexes with Schiff base ligands have been studied as antimicrobial and anticancer agents. Because of the capability to possess unusual configurations and biological importance, Schiff base complexes derived from amino acids are considered to be significant [1-4].

Schiff bases have been considered to be dominant intermediates in a number of enzymatic reactions such as interaction of an enzyme with an amino or carbonyl group of the substrate. Transaminases are spotted in mitochondria and cytosole of eukaryotic cells [5].

Polydentate ligands like Schiff bases, assisted by metal ions, compose highly organized supramolecular metal complexes. Such complexes are capable of binding sites and cavities for several cations, anions and organic molecules [6-8]. Lian et al. by using Single-crystal diffraction analysis revealed that all the complexes were mononuclear molecules, in which the Schiff base ligand showed different coordination modes and conformations. Also, they investigated the anticancer activity of the complexes and they concluded that complex, with salicylic acid as the auxiliary ligand, exhibited a stronger anticancer activity, referring to the fact that a synergistic effect of the Schiff base complex and the nonsteroidal anti-inflammatory drug may be involved in the cell killing process. The biological features of mixed-ligand copper(ii) Schiff base complexes and how acetic auxiliary ligands manipulate these features were also investigated [8-18] Abu-Khadra et al investigated the Antimicrobial Activity of Schiff Base (E)-N-(4-(2-Hydroxybenzylideneamino) Phenylsulfonyl) Acetamide Metal Complexes. Complexes were screened for their antibacterial {Gram negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*)}, {Gram positive bacteria (*Bacillus subtilis* and *Sterptococcus pneumoniae*)} and antifungal (*Aspergillus fumigates* and *Candida albicans*) and the observed promising antimicrobial biological features (19). They aslo noticed that Co(II) and Ni(II) complexes have magnetic moment values 4.58 B.M. and 3.22 B.M. respectively which agrees well with the expected value for a high-spin Co(II) ion in an octahedral environment [19].

Schiff bases are defined as the compounds containing azomethine group (-HC=N-) which were first reported by Hugo Schiff in 1864 and formed by condensation of a primary amine with an active carbonyl compound, and generally take place under acid, base catalysis or with heat. They are important compounds possessing the pharmacological activities such as anti-malarial,

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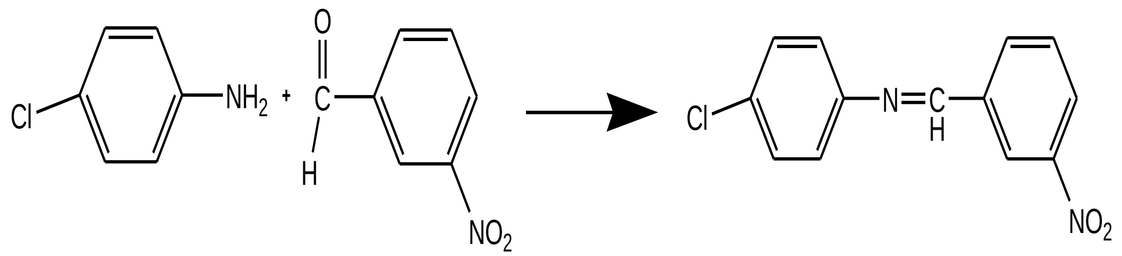
anticancer, antibacterial, antifungal, anti-tubercular, and anti-inflammatory [19]. Metal-chelate Schiff-base complexes have continued to play the role of one of the most important stereochemical models in main group and transition metal coordination chemistry due to their preparative accessibility, diversity and structural variability [20].
In another study, Azam et al performed a research and they investigated the synthesis and photoluminescent properties of a Schiff-base ligand and its mononuclear Zn(II), Cd(II), Cu(II), Ni(II) and Pd(II) metal complexes. The Schiff base displayed photoluminescence originating from intra-ligand (π–π*) transitions. According to the obtained results, Metal-mediated fluorescence quenching occurs in Cu(II), Ni(II) and Pd(II). The IR spectrum of the Schiff base proved characteristic bands for C,N, C,O and C–O vibrations [20]. Azam et al demonstrated the coordination ability of the ligand in complexation reaction with metal (II) ions [me- tal = Zn(II), Cd(II), Cu(II), Ni(II) and Pd(II)] (20). Lei et al have done a study on Zinc(II) and copper(II) 1D coordination polymeric complexes of a reduced Schiff base ligand. According the results of their study, The different coordination geometries of Cu (II) and Zn(II) show significant influence on the polymeric structures (21). According to another research, the IR, UV and EPR spectral investigations lead to the notion that the nickel and copper complexes show the octahedral and tetragonal geometries [22].
Gull et al. review the synthesis of Schiff base ligand derived from N-(1-Naphthyl) ethylenediamine with 1,2diphenylethane-1,2-dione in the ratio of 1:2 and its metal complexes. By observing Schiff base ligand and its metal complexes against bacterial and fungal strains and their preliminary results showed they showed that these complexes inhibited bacterial/fungal growth to a greater extent than the ligand [23]. The antimicrobial screening results of the synthesized ligand and its metal complexes indicated antimicrobial properties [23]. Soboia et al. (2014) performed a survey on antibacterial activity of copper (II) complexes of some ortho-substituted aniline Schiff bases. In their study, the Schiff base ligands were synthesized on the basos of the general procedure by condensing o- vanillin and salicylaldehyde with 2-chloroaniline, 2-bromoaniline, 2-methylaniline and 2-methoxyaniline, respectively [23]. They observed that the existence of the Cu(II) ions did not improve the antimicrobial activity of the free ligands. The copper complexes exhibited low level activity, compared to Schiff base ligands [23].
Imidazole-2-carboxaldehyde with amino acids derivatives are said to have analgesic, anti-inflammatory, anticancer and herbicidal activities. Some Schiff base complexes containing N and O donor atoms are effective as stereospecific catalysts for oxidation, reduction, hydrolysis, biocidal activity other organic and organic transformations [10, 11]. Beside what mentioned so far, it is important to mention that, some of these complexes have been shown to have interesting physical, chemical and potentially useful chemotherapeutic properties [12-16].
Accordingly, we are reporting the synthesis and characterization of complex derivatives including 3nitro benzaldehyde an para choloroaniline copper (II) chloride. Beside these, antibacterial activities of the complex obtained are fulfilled and the results are reported here.

Materials & Methods

Ligand syntheses by 3-nitro benzaldehyde and para choloroaniline: For the synthesis's ligand (1mmol) 3-nitro benzaldehyde solution in 5cc ethanol (5 min) and para choloroaniline (1mmol) solution in 5cc ethanol(5min). Then the two are mixed together for 10 min. The ligand to be synthesized.
With regard to figure 2, we want the synthesis of this ligand-ligand complex is needed to build this type of Schiff base ligands that have many applications including Katalyt, antibacterial materials, and so on.
Complex Syntheses by $CuCl_2$:

For the preparation of the title compound, a solution of N-(3-nitrobenzylidene)-4-cholorobenzenamine (0.269 g, 1.00 mmol) in ether (10 ml) was added slowly to a solution of CuCl2 (0.134 g, 1.00 mmol) in ethanol (10 ml) and the resulting yellow solution was stirred for 45 min at room temperature.



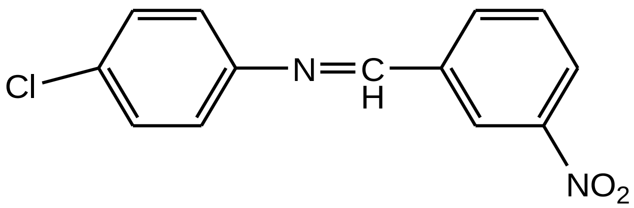


Figure 1: Synthesized ligand N-(3-nitrobenzylidene)-4-cholorobenzenamine

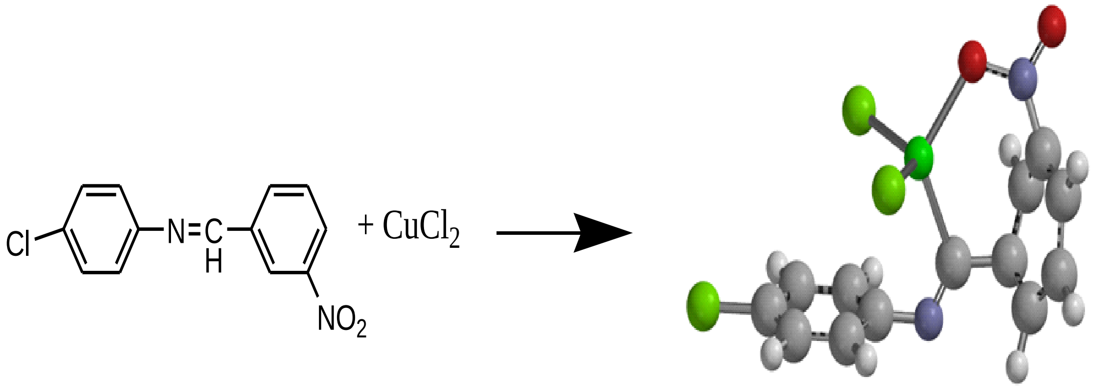


Figure 2: Reaction formation complex between salt Cu(II) and ligand

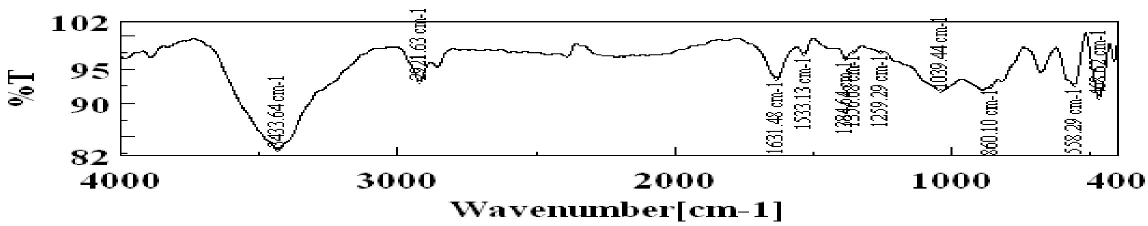


Figure 3: Spectrum IR Complex

We need the spectrum of figure 3 for verifying the complex.

Table (1) presents the peak figures and related descriptions.

Table1: Results of IR spectrum

Stretching Vibration of C=N	Stretching Vibration of C-H	Stretching Vibration of C=C	Flexural Vibration ofC-H
1631Cm^{-1}	3433Cm^{-1}	1295-1384Cm^{-1}	860Cm^{-1}

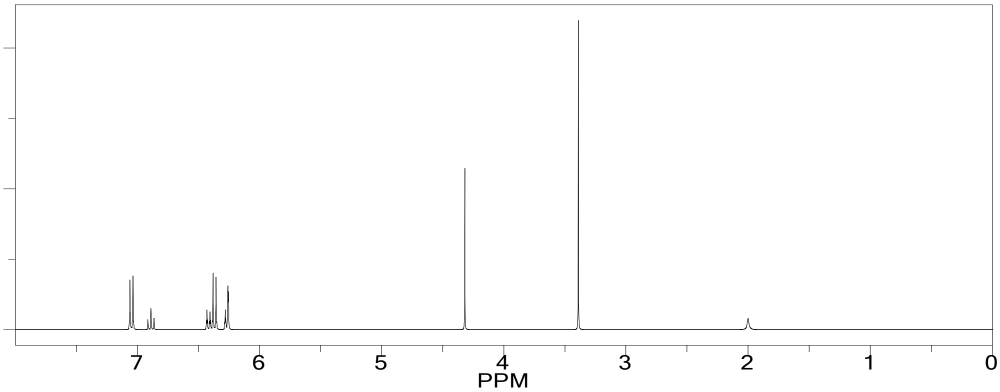


Figure 4: Spectrum HNMR complex

The values of HNMR are as follows:

Protocol of the H-1 NMR Prediction:

Node	Shift	Base + Inc.	Comment (ppm rel. to TMS)
CH	7.05	7.26	1-benzene
		0.01	1 -Cl
		-0.22	1 -N-C
CH	6.37	7.26	1-benzene
		-0.06	1 -Cl
		-0.83	1 -N-C
CH	6.37	7.26	1-benzene
		-0.06	1 -Cl
		-0.83	1 -N-C
CH	7.05	7.26	1-benzene
		0.01	1 -Cl
		-0.22	1 -N-C
CH2	4.32	1.37	methylene
		1.22	1 alpha -1:C*C*C*C*C*C*1
		1.73	1 alpha -N-1:C*C*C*C*C*C*1
CH	6.26	7.26	1-benzene
		-0.20	1 -C
		-0.80	1 -N
CH	6.27	7.26	1-benzene
		-0.19	1 -C
		-0.80	1 -N
CH	6.89	7.26	1-benzene
		-0.12	1 -C
		-0.25	1 -N
CH	6.42	7.26	1-benzene
		-0.20	1 -C
		-0.64	1 -N
OH	2.0	2.00	alcohol
CH3	3.39	0.86	methyl
		2.53	1 alpha -O

In accordance with Figs. 4 and 3, the region of 8.19ppm indicates the hydrogen imin. the regions of 7.52-8.16ppm indicates the hydrogens Aromatic. the region of 3.33ppm indicates the hydrogens methyl.

Based on Fig. 4, the region of 15ppm indicates the carbon methyl. the region of 28ppm indicates the carbon methylene. the region of 156ppm indicates the carbon imine. the regions of 115-128ppm indicates the carbons Aromatic. the regions of 137-151ppm indicates the carbons pyridine.

2.2. Antibacterial activity of cu complex

The antibacterial effect of this complex against *E.coli* was investigated by microdilution method. *E.coli* : 25922 from Azad university of center Tehran was used. The serial dilutions (1:2 to 1:1024) of cu complex and free cu with different concentration were prepared in nutrient broth. Then 1.5×10^{8} CFU/ml of *E.coli* suspension was added to each tube and incubated at 37 ºC for 16 h.

Then, the tubes were examined for turbidity, indicating the growth of microorganism. The lowest concentration of this complex that inhibited growth of *E.coli*, as detected by the lack of visual turbidity, was designated as MIC. The lowest concentration of complex that allowed survival of less than 0.1% of the original inoculums was assigned as MBC.

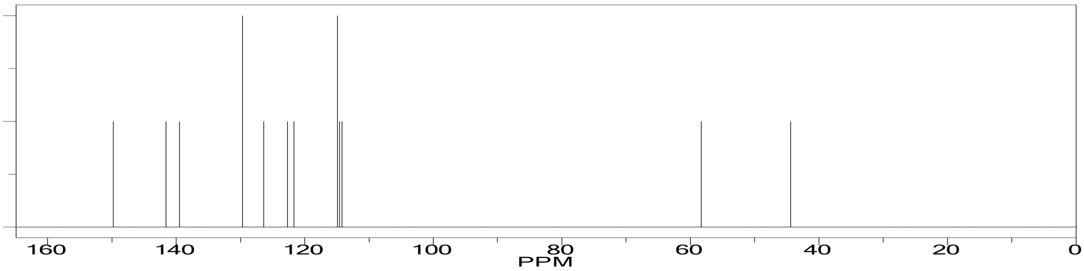


Figure 5: Spectrum CNMR Complex

The values of CNRM are as follows:

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Protocol of the C-13 NMR Prediction:

Node      Shift     Base + Inc.    Comment (ppm rel. to TMS)

  C       122.7        128.5       1-benzene
                         5.3       1 -Cl
                       -11.6       1 -N-C
                         0.5       general corrections
 CH       129.7        128.5       1-benzene
                         0.4       1 -Cl
                         0.8       1 -N-C
 CH       114.9        128.5       1-benzene
                         1.4       1 -Cl
                       -16.2       1 -N-C
                         1.2       general corrections
  C       141.6        128.5       1-benzene
                        -1.9       1 -Cl
                        15.0       1 -N-C
 CH       114.9        128.5       1-benzene
                         1.4       1 -Cl
                       -16.2       1 -N-C
                         1.2       general corrections
 CH       129.7        128.5       1-benzene
                         0.4       1 -Cl
                         0.8       1 -N-C
CH2        44           -2.3       aliphatic
                        24.3       1 alpha -1:C*C*C*C*C*C*1
                        28.3       1 alpha -N
                         9.3       1 beta -1:C*C*C*C*C*C*1
                         ?         1 unknown beta substituent(s)
                       -10.2       2 gamma -Cl
                         0.0       1 delta -N
                        -5.0       general corrections
                                   -> 1 increment(s) not found
  C       139.5        128.5       1-benzene
                        13.9       1 -C-N
                        -2.2       1 -N-O
                        -0.7       general corrections
 CH       114.2        128.5       1-benzene
                        -1.4       1 -C-N
                       -13.1       1 -N-O
                         0.2       general corrections
  C       149.8        128.5       1-benzene
                        -0.2       1 -C-N
                        21.5       1 -N-O
 CH       114.6        128.5       1-benzene
                        -2.0       1 -C-N
                       -13.1       1 -N-O
                         1.2       general corrections
 CH       126.4        128.5       1-benzene
                        -0.2       1 -C-N
                        -2.2       1 -N-O
                         0.3       general corrections
 CH       121.7        128.5       1-benzene
                        -1.4       1 -C-N
                        -5.3       1 -N-O
                        -0.1       general corrections
CH3        58.3         -2.3       aliphatic
                        49.0       1 alpha -O
                        11.3       1 beta -N
                        -2.6       1 gamma -1:C*C*C*C*C*C*1
                        -6.2       1 gamma -O
                         9.1       general corrections
```

Fig 6. Macrodilution method for MIC and MBC determiation

In the above figures, the cultivation environment of bacteria for MIC and MBC tests are showed.

Result and discussion

According to Fig. 1, the band of 3346 cm^{-1} is related to frequency of C-H Aromatic. The band of 1631 cm^{-1} is respected to C=N which is verified the imine. The bands of 1300-1533 cm^{-1} is related to the C=C benzene. The strong bands of 400-558 cm^{-1} is related to the bending frequency of Aromatic.

In accordance with Figs. 2, the region of 8.49ppm indicates the hydrogen imine. the regions of 7.58-8.17ppm indicates the hydrogens Aromatic. the region of 2.24ppm indicates the hydrogens methyl.

Based on Fig. 3 and 4, the region of 13.8ppm indicates the carbon methyl. the region of 19.8ppm indicates the carbon methylene. the region of 149.62ppm indicates the carbon imin. the regions of 116-129ppm indicates the carbons Aromatic. the regions of 149.06-149.62ppm indicates the carbons pyridin.
According this study MIC of the new complex was 0.005 µg/ml and its MBC 0.0025 µg/ml.
These findings showed enhanced antibacterial effect of new complex in comparison with free cu(II).

Due to increased antibacterial properties of copper(II). And we conclude that the copper coordination by ligand increases properties antibacterial. also when substituted in the ortho position is more impressive is the impact
Chemical compounds can destroy of microorganism by denaturation of organic compounds. This events are achieved by connection to functional groups .
Antibiotics:
Mechanism of action of antibiotics is following by below ways:
1. Inhibition of cell wall biosynthesis.
2. Inhibition of DNA function.
3. Inhibition of protein synthesis.
4. Inhibition of cytoplasmic membrane.
5.Metabolitic analogues (17).
At this experiment antibacterial susceptibility test of this complex was achieved by microdilution method. The results showed that the complex is formed. When the complex is formed and increases its anti-bacterial effect.

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