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Synthesis, Characterization, and Antibacterial Evaluation of Novel Binuclear Co(II) Complex Based on Thiosemicarbazone Derivative

Shahnaz Abdulhamid Hamad*[1], Hikmat Ali Mohamad[2], Rezan Ali Saleh[3] and Hero Farhad Salah[4]

[1]Department of General Science, College of Basic Education, Salahaddin university-Erbil, shahnaz.hamad@su.edu.krd , Erbil, Iraq
[2]Department of Chemistry, College of Education, Salahaddin university-Erbil, hikmat.mohamad@su.edu.krd
[3]Department of Chemistry, College of Education, Salahaddin university-Erbil, rezan.saleh@su.edu.krd, Erbil, Iraq
[4]Department of Biology, College of Education, Salahaddin University -Erbil, hero.salah@su.edu.krd, Erbil, Iraq
***Corresponding author email: Shahnaz.hamad@su.edu.krd**

تحضير وتشخيص والفعالية المضادة للبكتيريا لمركب ثنائي النواة كوبالت (11) الجديدة المعتمدة على مشتقات ثايوسيميكاربازيد ايستين

شاهناز عبد الحميد حمد [1], حكمت علي محمد [2] , ريزان علي صالح[3], هيرو فرهاد صالح [4]

[1]قسم العلوم العامة، كلية التربية الاساس، جامعة صلاح الدين–اربيل، shahnaz.hamad@su.edu.krd ، اربيل، العراق
[2]قسم الكيمياء، كلية التربية ، جامعة صلاح الدين–اربيل، hikmat.mohamad@su.edu.krd ، اربيل، العراق
[3]قسم الكيمياء، كلية التربية ، جامعة صلاح الدين–اربيل، rezan.saleh@su.edu.krd ، اربيل، العراق
[4]قسم البايوجي، كلية التربية ، جامعة صلاح الدين–اربيل، hero.salah@su.edu.krd ، اربيل، العراق

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ABSTRACT

Background: Extended exposure to antimicrobial drugs can lead to genetic changes in pathogens, resulting in resistance to specific antibiotics and posing significant public health challenges. This study aims to address this issue by synthesizing and characterizing a novel Co(II) complex with ((2,2'-(7,7'-dimethyl-2,2'-dioxo-1,1',2,2'-tetrahydro-3H,3'H-5,5'-biindole-3,3'-diylidene)dihydrazinecar bothioamide), denoted as ligand(L). The potential antibiotic activity of this complex is evaluated in vitro against three pathogens: E. coli ATCC 25922, P. mirabilis ATCC 14153, and S. pneumoniae ATCC 49619.

Methods: The novel Co(II) complex [Co_2 (L)Cl_2] was synthesized by reacting one mole of L with 2 moles of $CoCl_2$, yielding the general formula [Co_2LCl_2]. Characterization was performed using FT-IR, ^{1}H-NMR, UV-visible spectra, and elemental analysis (CHNS). The antimicrobial activity was evaluated by determining the Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC). Additionally, the synergistic effects of L and [Co_2(L)Cl_2] complex with ciprofloxacin (Cip) were tested against E. coli and P. mirabilis.

Results: The characterization confirmed the structure of the [Co_2(L)Cl_2] complex, indicating successful coordination via nitrogen, oxygen, and sulfur, exhibiting a square planar geometry. Both the L and [Co_2(L)Cl_2] complex exhibited antimicrobial activity against the tested pathogens. Additionally, when used in combination with ciprofloxacin, both the L and the [Co_2(L)Cl_2] complex showed synergistic effects against E. coli and P. mirabilis, with the [Co_2(L)Cl_2] complex exhibiting greater efficacy.

Conclusions: The novel [Co_2(L)Cl_2] complex demonstrated higher antimicrobial activity than the L and showed synergistic effects with ciprofloxacin against specific pathogens. As a result of this study, these two compounds show potential as antibacterial drugs.

Keywords: Antibacterial activity; Co(II) complex; Isatin moiety; Spectra.

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INTRODUCTION

The varied biological activities of isatin (indole-2,3-dione) and its derivatives have resulted in their widespread use as precursors for synthesizing numerous biologically active compounds. These compounds exhibit a range of activities, including antifungal[1-3], antibacterial [4, 5], antimycobacterial[3], analgesic [6], anti-HIV[7-9], and anticancer activity [1, 10-12]. Conversely, Thiosemicarbazones are studied extensively for their biological activities, including anticancer, antiviral, and antibacterial properties[13].The presence of N and S of the compounds may be responsible for their ability to inhibit the proliferation of various types of cancer cells and pathogens; hence, they are particularly notable in medicinal chemistry for their potential biological activity[14]. Since thiosemicarbazones have an excellent ability to chelate with a wide range of biologically relevant metal ions and form stable coordinate complexes, These complexes might exhibit increased biological activities compared to the thiosemicarbazones alone, and their mechanisms of action could be changed as a result[15, 16]. These complexes showed remarkable potential for inhibiting the growth of various pathogenic microorganisms[17, 18].

Recent research has highlighted metal complex-based antibiotics have shown better physicochemical properties and greater effectiveness than their parent drugs [19]. With continued exposure to antimicrobial drugs over an extended period, pathogens often undergo genetic changes within their cells, resulting the resistance to particular antibiotics[20]. This resistance will lead to a rise in multidrug-resistant organisms leading to severe public health challenges. For example, Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterococcus faecium, and Acinetobacter baumannii have become major concerns.[21] . Millions of individuals globally are underscoring the urgent need to address antibiotic resistance in medical research and public health policy each year.

Based on these facts, we present the synthesis and chemical characterization of isatin thiosemicarbazone derivatives complex with the empirical formula $C_{20}H_{18}N_8O_2S_2$ (L) and its novel complex with the Co(II) metal; empirical formula $C_{20}H_{16}Cl_2Co_2N_8O_2S_2$ $[Co_2(L)Cl_2]$. The structures were confirmed using IR, ^{1}H NMR, and UV-visible spectroscopy. The synthesized complexes were investigated for antibacterial properties against the three pathogens (*E. coli* ATCC 25922, *P. mirabilis* ATCC14153 and *S. pneumoniae* ATCC 49619. Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) have also been evaluated. Synergistic effects were observed between ligand or $[Co_2(L)Cl_2]$ complex and ciprofloxacin against E. coli ATCC 25922 and P. mirabilis ATCC 14153.

MATERIALS AND METHODS

All chemicals are of reagent grade and are used as specified (Fluka), (Merk), (Alpha), or (B.D.H). The Shimadzu FT-IR. 8400 spectrometer was used to record infrared spectra in the (400-4000) cm^{-1} range. Elemental analysis was performed on the (LECO CHNS-932). The metal analyses were performed using a Perkin Elmer OPtema 7300DV ICP-OES Spectrometer. Complex ^{1}H-NMR spectra were acquired using a Bruker ultra shield 300 MHz with TMS as an internal reference at Mashhad University in Iran. The melting point was measured with the Melting Point-MPD-100Pixel Technology CO., Limited. The conductivity measurements were recorded using a SenzSiemen conductivity tester. Shimadzu's AE-UV1609 (UK) CO., LTD was

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used to capture electronic transition spectra in the (200-800) nm region. Bacterial suspensions (*E. coli* ATCC 25922, *P. mirabilis* ATCC14153, and *S. pneumoniae* ATCC 49619, all were purchased from Medya Diagnostic Center, Erbil-Kurdistan Region of Iraq)

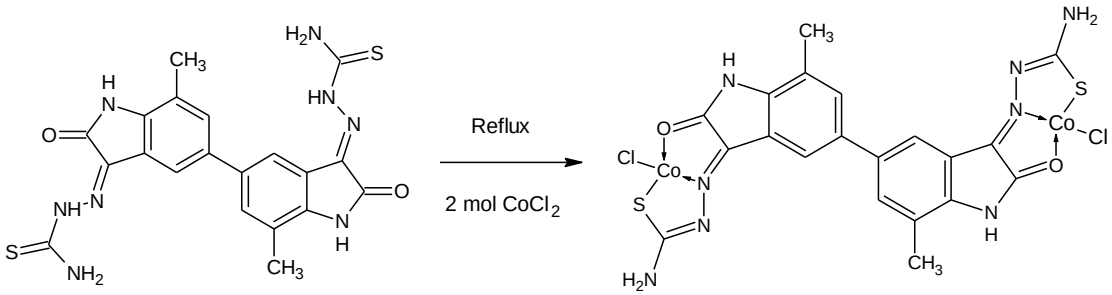
Preparation of the complexes:

Synthesis of ligand (L): 2,2'-(7,7'-dimethyl-2,2'-dioxo-1,1',2,2'-tetrahydro-3H,3'H-5,5'-biindole-3,3'-diylidene)dihydrazinecarbothioamide.

The synthesis of the ligand is described by Hamad[22].

Synthesis of the $[Co_2(L)Cl_2]$ complex:

(1 mole) of the Ligand (L) was refluxed with (2 moles) of $CoCl_2.6H_2O$ for 2 hours at 50-60 °C. (Scheme 1). The formed precipitate was filtered off and rinsed with cold ethanol. Table 1 summarizes the physical properties of the end products.



Ligand (L) $[Co_2(L)Cl_2]$

Scheme 1

Table 1: Physical properties and analytical data of ligand and its complex

No	Complex	Color	Yiel d%	M.Wt g/mol	d.P. (°C)	(Calculated) Found % C	H	N	M
1	L*	Brawn	65%	466.54	238.6	(51.49) 52.08	(3.89) 3.96	(24.02) 24.82	….
2	$Co_2(L)Cl_2$	Reddish brown	75%	653.3	>300	(36.77) 35.81	(2.47) 3.22	(17.15) 18.0	(18.04) 18.50

* published [22]

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RESULTS AND DISCUSSION

Chemistry

Infrared spectroscopic study:

Table 2 lists selected vibrational bands of the ligand and the two metal complexes. When the spectra of Schiff bases are compared, the complexes exhibit a band at 3190–3155 cm^{-1}, corresponding to the υ(N-H) stretching mode of the amide group for the ligand (L) and the cobalt complex, respectively. Aromatic C-H stretching was assigned to the bands appearing near 3062 cm^{-1} for the ligand and 3061 cm^{-1} for the cobalt complex, while aliphatic C-H stretching was assigned to the bands observed near 2817 cm^{-1} for the ligand and 2954 cm^{-1} for the cobalt complex. The υ(C=O) vibration is assigned to the bands at approximately 1693 cm^{-1} and 1637 cm^{-1} for the ligand and the cobalt complex, respectively. The band shift to lower wavenumbers indicates that the carbonyl oxygen atom is coordinated with the metal ion[23]. The υ(C=N) band at 1622 cm^{-1} for the ligand is shifted to a lower wavenumber (1560 cm^{-1}) in the cobalt complex, signifying that the nitrogen of the azomethine group is coordinated to the metal ion. In the spectrum of the ligand, the υ(N-N) band occurred at 1153 cm^{-1}, but during complex formation, this band shifted to a lower frequency (1083 cm^{-1}), indicating the participation of the nitrogen atom in complexation [24].

The band corresponding to the C=S stretch shows at 819 cm^{-1} in the spectra of the ligand. while in the complex is reduced to 698 cm^{-1} indicating the coordination of S- atom to the metal ion This coordination is further supported by the presence of new bands at 439 cm^{-1}, attributed to the υ(M-N) band [25].

The IR spectrum results support the tridentate complexation of the Schiff base with metal ions. The infrared spectrum for the synthesized complexes is shown in Figure 1.

Table 2: The selected IR spectra bands (cm^{-1}) of the free ligand and its complex

Comp.	υ N-H	C-H str. Aleph.	C-H str. Arom.	υ C=O	υN-N	υC=N	υ C=S	υ C-S	υ M-S
L*	3190	2877	3062	1693	1153	1622	819	…..	……-
$Co_2(L)Cl_2$	3151	2954	3061	1637	1083	1560	…..	698	435

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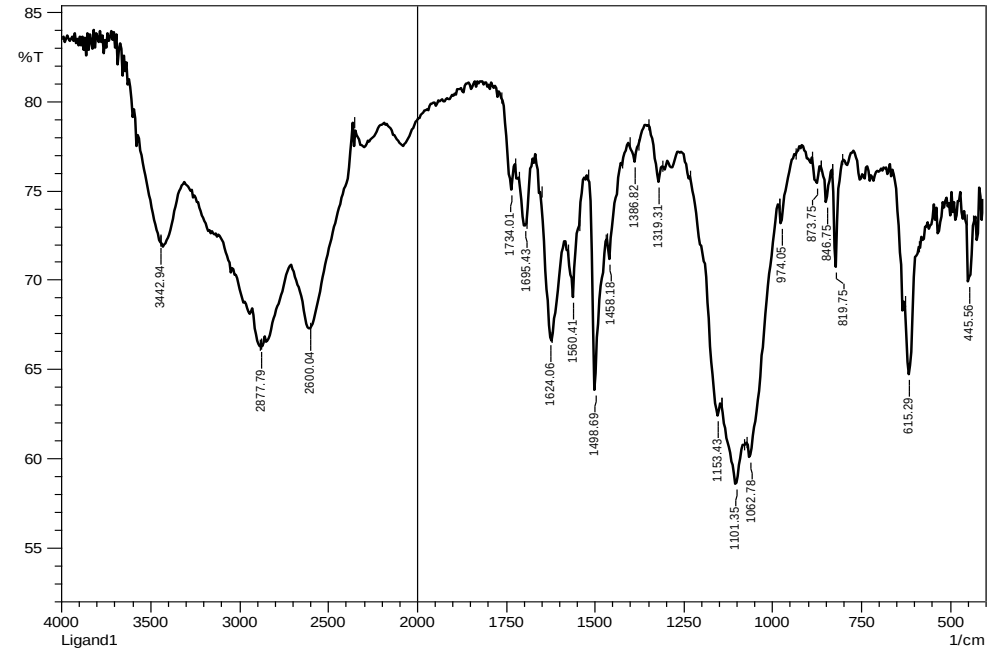
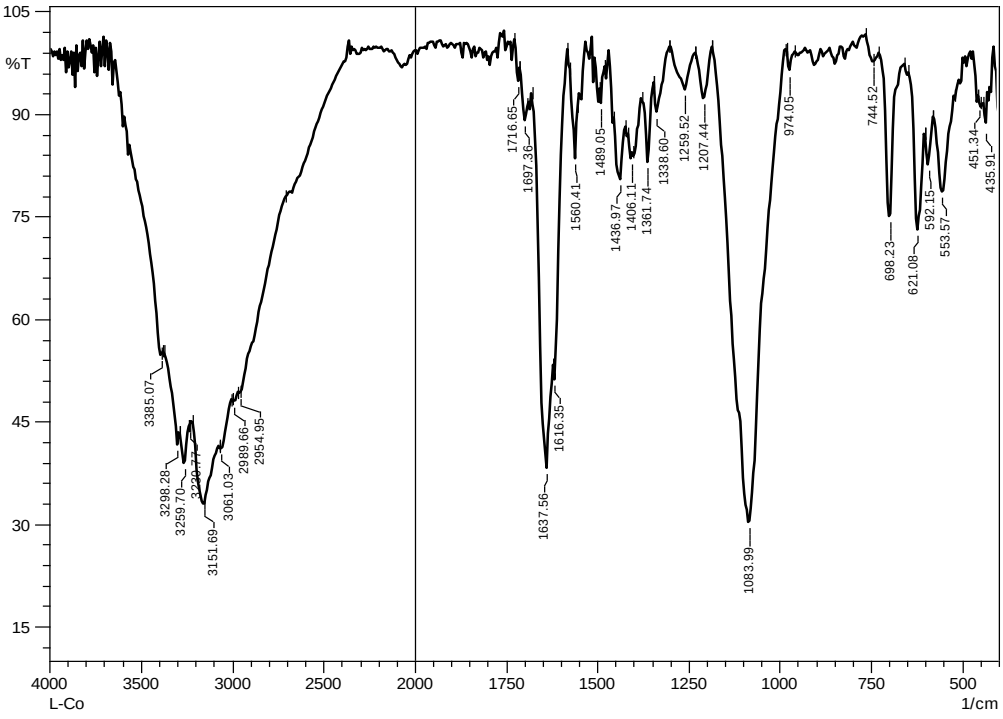


A



B

Figure 1: The Infrared spectra A of (L)[22] and B of $[Co_2(L)Cl_2]$.

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^{1}H-NMR data :

Figures. 2 and 3 show the ^{1}H-NMR spectra of substances ((L)[22] and $[Co_2(L)Cl_2]$ in DMSO, with peak assignments given in Table 3. In the DMSO solution, the 1H-NMR spectra of the complexes (L and $[Co_2(L)Cl_2]$) were recorded. The findings revealed that the signals at (11.36, 11.35) attracted the N-H proton of isatin for L and $[Co_2(L)Cl_2]$), respectively. Aromatic ring protons were found at 7.36 and 7.45 for L and $[Co_2(L)Cl_2]$) respectively. Finally, the methyl group of indole emerged as a singlet at 2.51 for both ligand and its complex

Table 3: Assignment of ^{1}H-NMR spectral data of compounds

No.	Compound	(δ) in ppm (multiplicity, intensity, assignment)
1	L*	11.36(s,3H,NH), 7.36(m,6H,ArH), 7.08(S,2H,=CH), 2.51(s,6H,Ar-CH_3)
2	$[Co_2(L)Cl_2]$	11.35(s,2H,NH), 7.45(m,6H,ArH), 2.51(s,6H,Ar- CH_3)

L*published[22]

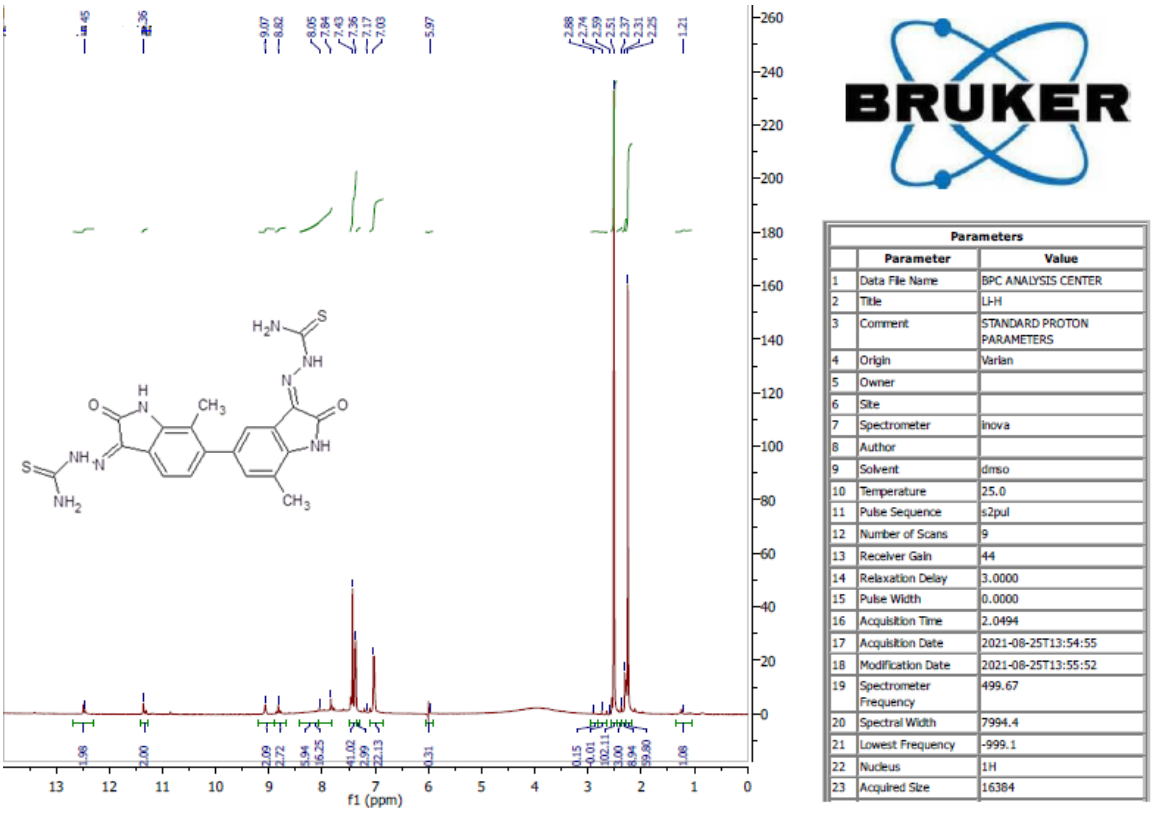

Figure 2: ^{1}H-NMR of (L) ligand.[22]

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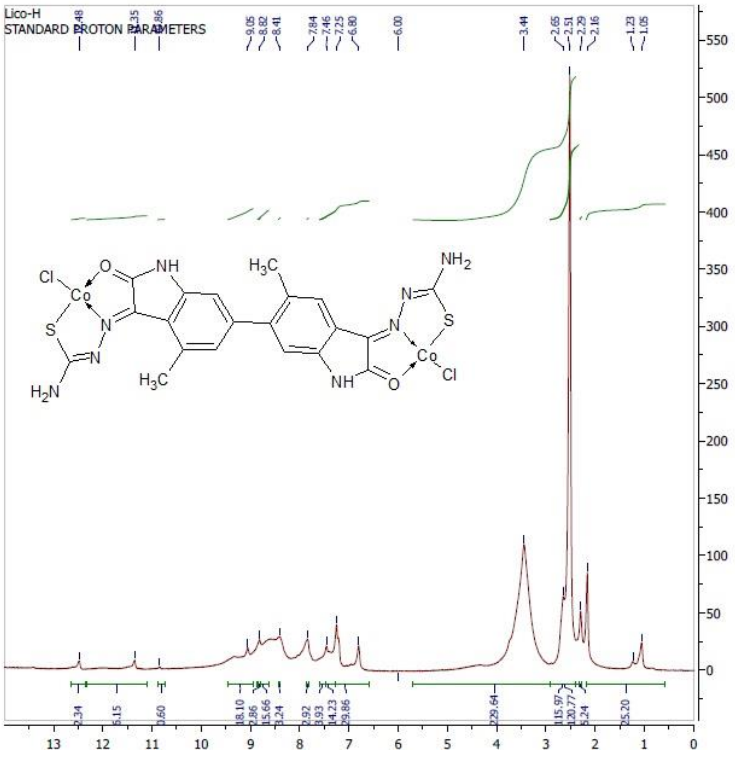

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18	Modification Date	2021-08-25T13:31:28
19	Spectrometer Frequency	499.67
20	Spectral Width	7994.4
21	Lowest Frequency	-999.1
22	Nucleus	1H
23	Acquired Size	16384

Figure 3: ^{1}H-NMR of $[Co_2(L)Cl_2]$

Conductivity measurement

The molar conductivity values of the ligand and the Co(II) complex in DMSO solvent at 25℃ are 24 and 30 (Ω^{-1} cm^2 mol^{-1}), respectively, indicating that both ligand and its cobalt complex exhibit non- electrolytic behaviour (Table 4).

Electronic spectral studies

The electronic spectra of the ligand[22] and the Co complex $[Co_2(L)Cl_2]$ in 10^{-3} M solution DMSO were recorded, and the results were listed in Table 4, giving two peaks of Ligand (L), at 33783, 26178 cm^{-1}, which are assigned to the π- π* and n-π* transitions inside the ligands, respectively. The UV-visible spectra of $[Co_2(L)Cl_2]$ complex gave four spins permitted transitions at 38314, 34129, 32679 and 26595 cm^{-1}, which were ascribed to π→π*, C.T., C.T, $^{4}T_{1g(F)} \rightarrow {}^{4}T_{1g(P))}$ respectively. It's feasible to assign square planar geometry. [25], [26].

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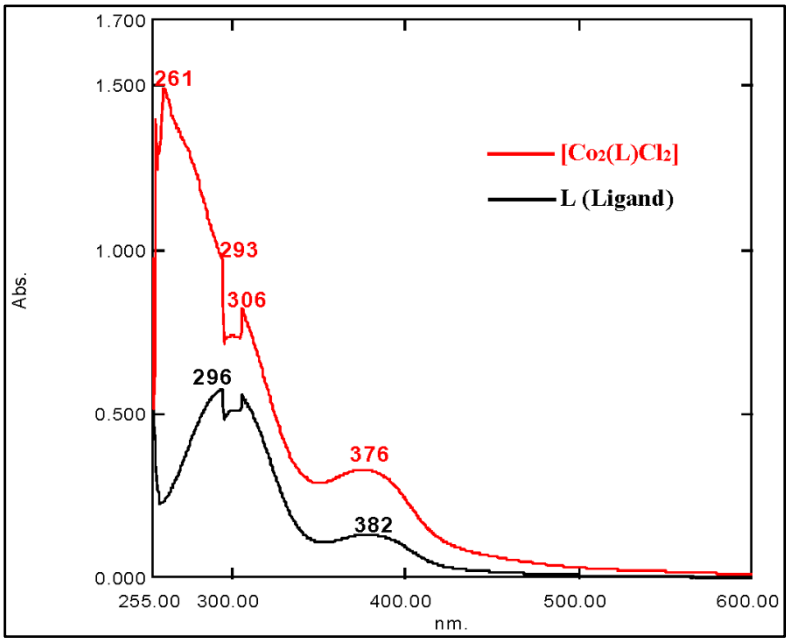

Figure 4: Electronic spectrum of Ligand (L)[22] and $[Co_2(L)Cl_2]$

Table 4: Electronic spectra and molar conductivity of the ligand and its complex

Compounds	Absorption band		Transition assignment	ε_{max} (L.mol^{-1} cm^{-1})	Molar conductivity (ohm^{-1}.cm^2.mol^{-1})
	nm	cm^{-1}			
L*	296	33783	π→π*	578	24
	382	26178	n→π*	122	
L-Co	261	38314	π→π*	1481	30
	293	34129	C.T.	987	
	306	32679	C.T	813	
	376	26595	$^4T_{1g(F)} \rightarrow {}^4T_{1g(P)}$	319	

L* Published [22]

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Antibacterial activity

Materials and Methods

Preparation of inoculums

Bacterial suspensions (*E. coli* ATCC 25922, *P. mirabilis* ATCC14153 and *S. pneumoniae* ATCC 49619, all were purchased from Medya Diagnostic Center, Erbil-Kurdistan Region of Iraq) were prepared according to 0.5 McFarland standard. A 24-hour old culture was used to prepare the bacterial suspensions. The organism was suspended in sterile normal saline, and the turbidity was adjusted to approximately 1 x 10^8 cfu/ml by aligning the optical density of the bacterial suspension with the 0.5 McFarland turbidity standard [27].

5.1.3 Sterility test of the ligand and ligand complex

Ligand and $[Co_2(L)Cl_2]$ complex were tested for the growth of microbes. This was carried out by inoculating 0.1ml of each of them on sterile Mueller Hinton Agar (MHA) and incubating at 37 ˚C for 18–48 hrs. The plates were observed for growth. The absence of growth on the inoculated plates after incubation indicates sterility of ligand and ligand complex and is evaluated for antibacterial activity.

Antibacterial activity by using well diffusion assay

To evaluate the activity of the ligand and $[Co_2(L)Cl_2]$ complex against three reference bacterial strains (*E. coli* ATCC 25922, *P. mirabilis* ATCC14153) Gram negative and (*S. pneumoniae* ATCC 49619) Gram positive, Muller-Hinton agar plates (MHA) were cultured with 0.1 ml of prepared inoculums, adjusted to 0.5 McFarland turbidity standard of tested bacteria. The inoculums were spread using a sterile swab to achieve confluent growth. After allowing the plates to dry, a sterile cork borer with an 8.0 mm diameter was used to create four wells in each agar plate. Approximately 100 µl of the ligand and the [Co2(L)Cl2] complex were separately added to the wells, each containing a determined concentration. Positive controls (ciprofloxacin 10 µg/ml and nitrofurantoin 10 µg/ml) and negative controls (5% DMSO and sterile distilled water) were also included. The plates were then incubated for 24 hours at 37 ºC, and the zones of inhibition were measured to the nearest millimeter (mm)[28]. The experiment was performed in triplicates.

Minimum inhibitory concentration (MIC)

The MIC of the ligand and $[Co_2(L)Cl_2]$ was determined by serial twofold dilution in 96-well plates, according to the Clinical and Laboratory Standards Institute (CLSI) guidelines [29]. Briefly, 100 µl of Mueller Hinton broth was added to all wells, then,100 µl of ligand and $[Co_2(L)Cl_2]$ was poured into well A-1; the wells A2-A7 used to make sequential dilution relative to well A-1 (33 to 0.4843 mg/ml). All wells were added with 10 µl of diluted reference strain cultures equal to $5*10^5$ cfu/ml. Five control wells were maintained for each strain (medium control, organism control, ligand/$[Co_2(L)Cl_2]$ complex control, standard antibiotic control, and DMSO 5% solvent control). The microtiter plates were incubated at 37 °C for 24 h. The lowest concentration (highest dilution) of the chemical that produced no visible growth (no turbidity) in 24 h when compared with the control tubes was considered as MIC.

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Synergistic Antibacterial Assays

To determine the synergistic antibacterial activity of the ligand and $[Co_2(L)Cl_2]$ complex, the method described by Sulieman et al, [30] was followed with some modification; ciprofloxacin was used in combination with ligand and $[Co_2(L)Cl_2]$ complex. The reference strains were spread with a turbidity of 0.5 McFarland on (MHA) plates. For the assessments of the synergistic effects, the selected antibiotic (10 µg/ml) was mixed with a ligand or $[Co_2(L)Cl_2]$ complex and employed in the wells of inoculated agar plates. The zones of inhibition produced by the ligand or ligand complex in combination with ciprofloxacin after overnight incubation were estimated as[31], the synergistic effect occurs when the combined effect of two drugs surpasses the impact of each drug individually. Indifference arises when the combined effect of two drugs equals the effect of either drug alone. Antagonism occurs when the combined effect of two drugs is weaker than the effect of each drug alone.

Minimum bactericidal concentration (MBC)

MBC of ligand and $[Co_2(L)Cl_2]$ was performed by taking 10 µl from the micro-broth well obtained from the MIC experiment (which provided the MIC value) along with three wells above the MIC value well and spreading them onto (MHA) plates. The colonies were counted after incubating for 18–24 hours at 37°C. The concentration of the sample that produces either no growth or the growth of 3-4 colonies was considered the MBC value. The MBC is defined as the lowest concentration of the chemical capable of killing 99.9% of the bacterial inoculum after 24 hours of incubation at 37°C [32].

RESULTS AND DISCUSSION:

Table 5 and Figure 5 show the activity of both ligands alone and ligand in combination with Co as broad-spectrum antibacterial agents against Gram negative (*E. coli* ATCC 25922, *P. mirabilis* ATCC 14153) and Gram positive (*S. pneumoniae* ATCC 49619). It appeared that these agents had a strong effect on inhibiting bacterial growth, especially at the concentration of 33 mg/ml where the inhibition zone was 15, 20 and 18, 19 mm for ligand and ligand in combination with Co, respectively against *E. coli* ATCC 25922 and *P. mirabilis* ATCC 14153 respectively, and both agents inhibited growth of *S. pneumoniae* ATCC 49619 completely with all concentrations.

Furthermore, the results show that the Gram positive bacterium (*S. pneumoniae* ATCC 49619) was the most susceptible to both agents in comparison with Gram negative bacteria (*E. coli* ATCC 25922 and *P. mirabilis* ATCC 14153); this may return to the presence of an outer membrane (lipopolysaccharide), which has hydrophilic polysaccharide series that play as a barrier against hydrophobic screened agents [33].

On the other side, the results show that the ligand complex possesses a greater effect than the free ligand against *E. coli* ATCC 25922, and this can be explained based on Overtone's concept and Tweedy's chelation theory.

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Table 5: Antibacterial activity of Ligand and $[Co_2(L)Cl_2]$ against *E. coli* ATCC 25922, *P. mirabilis* ATCC 14153 and *S. pneumoniae* ATCC 49619

Agent Concentration mg/ml	***E. coli* ATCC25922**		***P. mirabilis* ATCC14153**		***S. pneumoniae* ATCC 49619**	
	Zone of Inhibition (mm)					
	Free ligand	**$[Co_2(L)Cl_2]$**	**Free ligand**	**$[Co_2(L)Cl_2]$**	**Free ligand**	**$[Co_2(L)Cl_2]$**
33	15	18	20	19	The growth was completely inhibited over the plate	
16.5	10.5	13	18	11		
8.25	9	-*	Less growth	-		
4.125	-	-	-	-		
Ciprofloxacin	41		43		36	
Nitrofurantoin	33		34		35	
DMSO 5%	-		-		-	
St.D.W.	-		-		-	

*:No effect

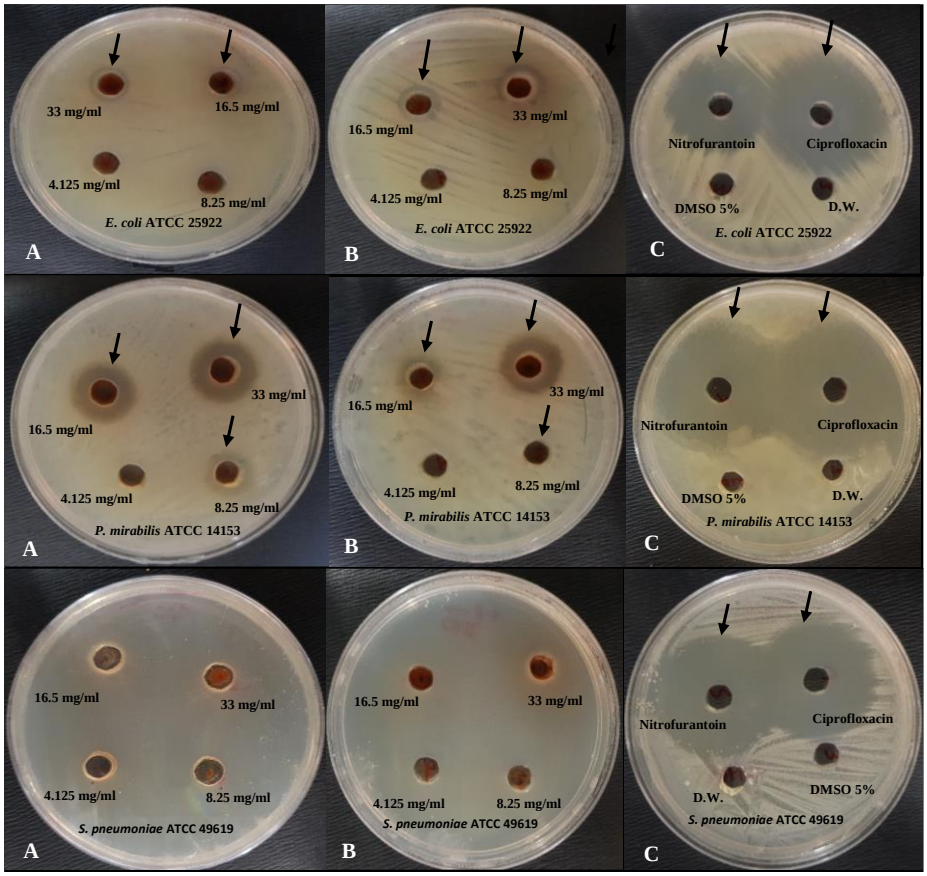

Figure 5: Antibacterial activity of ligand/$[Co_2(L)Cl_2]$ complex against bacteria under study, A: effect of ligand, B: effect of $[Co_2(L)Cl_2]$ complex, C: effect of Ciprofloxacin and Nitrofurantoin as +ve controls, and D.W. and DMSO as negative controls.

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Combination medication can be used to broaden the antibacterial spectrum, aid in preventing the emergence of resistant mutants, and obtain synergistic antibacterial activity. They present a viable alternative to mono-medication for patients facing challenging invasive infections, particularly those caused by multi-resistant species or individuals who fail to respond to standard treatment[31]. Therefore, the determination of synergistic effect between ligand, $[Co_2(L)Cl_2]$ complex, and antibiotic (Ciprofloxacin) was evaluated by comparing the size of the inhibition zone of ligand and $[Co_2(L)Cl_2]$ complex alone and Cip alone on the three strains under study with size of inhibition zone of ligand/$[Co_2(L)Cl_2]$ complex and Cip together (Table 6 and Figure 6) as results revealed that synergistic effects appear in ligand with Cip against growth of *E. coli* ATCC 25922. The effect was very strong, where there was no growth completely. Further, the synergistic interaction in combination of ligand complex with Cip against *E. coli* ATCC 25922 and *P. mirabilis* ATCC14153, whereas, the combination of the mentioned antibiotic and ligand complex with a concentration of (4.125 mg/ml) against mentioned two strains, was synergistic for ligand complex where when the complex was used alone it hadn't had any effect, and was antagonistic for antibiotic, where when the antibiotic was used alone, it had stronger effect in comparison with the combination. Furthermore, the synergistic effect is clear in the case of a combination of the ligand (33mg/ml and 16.5 mg/ml) and an antibiotic against *P. mirabilis* ATCC 14153, in contrast, it was synergistic for ligand where when the ligand was used alone (8.25 mg/ml and 4.125 mg/ml) it didn't had any effect and was antagonistic for antibiotics in combination with ligand. On the other hand, the effect of the ligand or ligand complex in combination with Cip was indifferent against *S. pneumoniae* ATCC 49619, because the effect of two drugs together is the same as ligand or ligand complex alone. Therefore, our finding is of important value, which shows that the combination of ligand or $[Co_2(L)Cl_2]$ complex and Cip could be considered for treatment of infections due to multidrug-resistant mentioned strains in this investigation after confirmation of their synergism by well diffusion method.

The mechanism of the synergy of these two drugs (ligand and $[Co_2(L)Cl_2]$ complex need to be investigated more. It might be illustrated that the composition of the mentioned drugs disturbs the cell wall or increases permeability of the cytoplasmic membrane, thereby facilitating the increased influx of antibiotics Additionally, they may act as efflux pump inhibitors or inhibit penicillin-binding proteins, although further research is needed to elucidate these mechanisms. Antibiotics in combination with these medications may serve as an important foundation for novel approaches to compounds that change resistance. Additional studies with a significant number of isolates are necessary to verify well diffusion as a technique for evaluating the synergistic combination of the ligand or $[Co_2(L)Cl_2]$ complex with antibiotics.

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Table 6: Antibacterial activity of the combination of Ligand ciprofloxacin and combination of $[Co_2(L)Cl_2]$ and ciprofloxacin against *E. coli* ATCC 25922, *P. mirabilis* ATCC 14153 and *S. pneumoniae* ATCC 49619

Agent Concentration mg/ml	***E. coli* ATCC25922**		***P. mirabilis* ATCC14153**		***S. pneumoniae* ATCC 49619**	
	Zone of Inhibition (mm)					
	Free ligand	**$[Co_2(L)Cl_2]$**	**Free ligand**	**$[Co_2(L)Cl_2]$**	**Free ligand**	**$[Co_2(L)Cl_2]$**
33	The growth was completely inhibited over the plate	50	44	45	The growth was completely inhibited over the plate	
16.5		45	42	45		
8.25		44	36	44		
4.125		35	13	9		
Ciprofloxacin	41		43		36	
DMSO 5%	-		-		-	
St. D.W.	-		-		-	

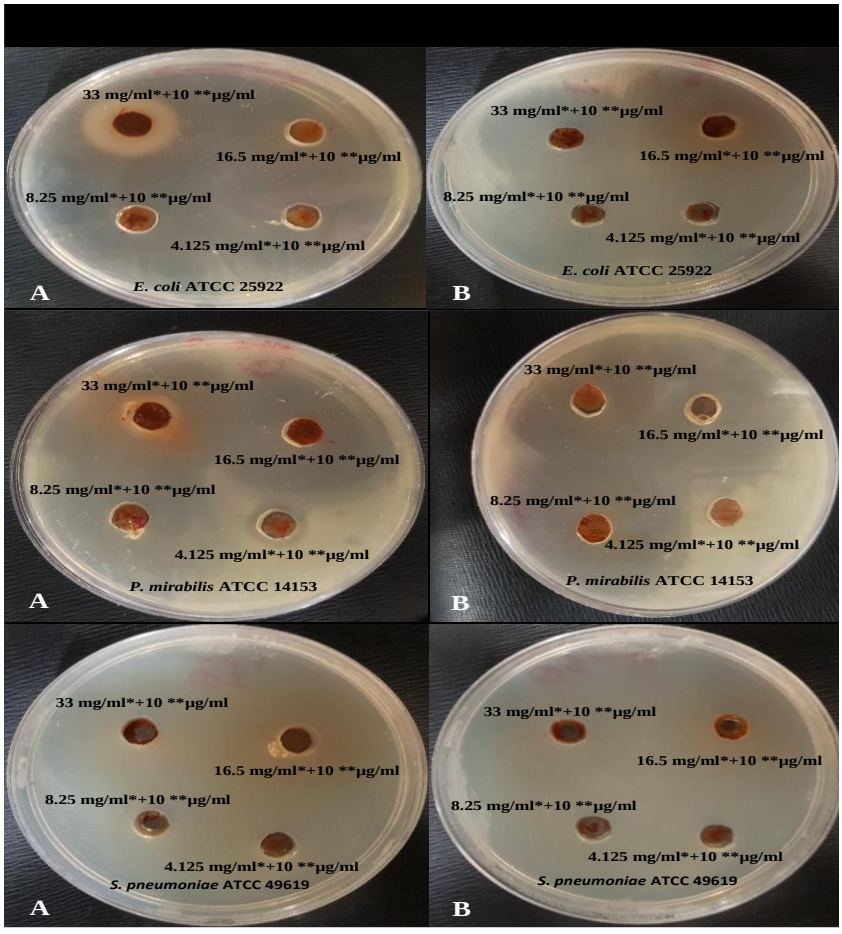

Figure 6: Antibacterial activity of ligand/$[Co_2(L)Cl_2]$complex in combination with ciprofloxacin against bacteria under study, A: effect of ligand+ ciprofloxacin, B: effect of $[Co_2(L)Cl_2]$complex+ ciprofloxacin, *: concentration of ligand or $[Co_2(L)Cl_2]$complex, **: concentration of ciprofloxacin.

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The MIC and MBC of ligand and ligand-Co were evaluated in this investigation (Table 7), where the MIC was 0.515625 mg/ml and 8.25 mg/ml and the MBC was 1.03125 mg/ml (ligand), 20625 mg/ml ($[Co_2(L)Cl_2]$ complex) and 16.5 mg/ml for *S. pneumoniae* ATCC 49619, and *E. coli* ATCC 25922, *P. mirabilis* ATCC 14153 respectively.

Table 7: MIC and MBC values of ligand and $[Co_2(L)Cl_2]$against *E. coli* ATCC 25922 *P. mirabilis* ATCC 14153 and *S. pneumoniae* ATCC 49619

Antibacterial agent	*E. coli* ATCC 25922		*P. mirabilis* ATCC 14153		*S. pneumoniae* ATCC 49619	
	MIC mg/ml	MBC mg/ml	MIC mg/ml	MBC mg/ml	MIC mg/ml	MBC mg/ml
Ligand	8.25	16.5	8.25	16.5	0.515625	1.03125
$[Co_2(L)Cl_2]$	8.25	16.5	8.25	16.5	0.515625	2.0625

CONCLUSION

Elemental and spectroscopic studies have validated the structure of the novel thiosemicarbazone derivative. According to the spectroscopic results, $[Co_2(L)Cl_2]$ exhibits a square planar geometry, with the metal ion coordinating with the ligand via nitrogen, oxygen, and sulfur centers. Both the ligand alone and its Co complex against various bacterial strains demonstrated a potent antimicrobial activity, $[Co_2(L)Cl_2]$ showed greater antimicrobial activity than the ligand. The MIC and MBC values further support the potent antibacterial activity of both the ligand and $[Co_2(L)Cl_2]$ complex. However, to establish these compounds as promising novel potential antibacterial drugs, further experiments must be done using advanced techniques against a wider range of pathogenic bacteria. These findings give positive support to further research to develop novel antibacterial drugs.

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Conflict of interests:

There is no conflict of interest

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الخلاصة

المقدمة:

التعرض الطويل للأدوية المضادة للميكروبات يمكن أن يؤدي إلى تغيرات جينية في مسببات الأمراض، مما يؤدي إلى مقاومة مضادات حيوية معينة ويشكل تحديات كبيرة على الصحة العامة. تهدف هذه الدراسة إلى معالجة هذه المشكلة من خلال تصنيع و معقد Co(II) الجديد مع ((2,2'-(7,7)-dihydrazinecar Bothioamide)، والمشار إليه باسم ligand(L) ويتم تقييم نشاط المضاد الحيوي المحتمل لهذا المركب في المختبر ضد ثلاثة مسببات الأمراض E :القولونية ATCC 25922 ، P. mirabilis ATCC 14153، و S. الرئوية ATCC 49619.

طرق العمل:

تم تصنيع مركب Co(II) الجديد $[Co_2(L)Cl_2]$ من خلال تفاعل مول واحد من L مع 2 مول من $CoCl_2$، مما أدى إلى الحصول على الصيغة العامة $[Co_2(L)Cl_2]$ تم إجراء التوصيف باستخدام FT-IR و ^{1}H-NMR والأطياف المرئية فوق البنفسجية والتحليل العنصري (CHNS). تم تقييم النشاط المضاد للميكروبات عن طريق تحديد الحد الأدنى للتركيز المثبط (MIC) والحد الأدنى لتركيز مبيدالجراثيم (MBC). بالإضافة إلى ذلك، تم اختبار التأثيرات التآزرية لمركب L و$[Co_2(L)Cl_2]$ مع السيبروفلوكساسين (Cip) ضد E. coli و P. mirabilis.

النتائج:

أكد التوصيف بنية معقد $[Co_2(L)Cl_2]$، مما يشير إلى التنسيق الناجح عبر النيتروجين والأكسجين والكبريت، مما يظهر هندسة مستوية مربعة. أظهر كل من معقد L و$[Co_2(L)Cl_2]$ نشاطًا مضادًا للميكروبات ضد مسببات الأمراض التي تم اختبارها. بالإضافة إلى ذلك، عند استخدامه مع سيبروفلوكساسين، أظهر كل من مركب L و$[Co_2(L)Cl_2]$تأثيرات تآزرية ضد *E. coli* و*P. mirabilis*، مع مركب $[Co_2(L)Cl_2]$ يُظهر فعالية أكبر.

الإستنتاجات:

أظهر المعقد الجديد [Co2(L)Cl2] نشاطًا مضادًا للميكروبات أعلى من المعقد L وأظهر تأثيرات تآزرية مع السيبرو فلوكساسين ضد مسببات أمراض معينة. ونتيجة لهذه الدراسة، أظهر هذان المركبان إمكانية استخدامهما كأدوية مضادة للبكتيريا.

الكلمات المفتاحية: نشاط . مضاد للجراثيم ، مركب(II) Co ، شاردة الإيساتين, أطياف.

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