

SYNTHESIS, STUDIES THEIR QUANTUM MECHANICAL PROPERTIES AND BIOLOGICAL ACTIVITY OF NEWER ANTIPYRIN DERIVATIVE AND ITS (CU²⁺) COMPLEX

E. H. Al – Tememe R. M. ,Al - Hrashawy

College of Pharmacy , University of Basrah, Basrah, Iraq.

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ABSTRACT

The synthesis of (C₁₆H₁₄N₃O₂) ligand and (Cu₂C₃₂H₂₈N₆O₁₂S₂) complex are prepared in this work . The newly prepared compounds were characterized by IR spectroscopy and elemental analysis . The determination of the antimicrobial activity of ligand and its complex was carried out on sample of Escherichia coli , Klebsiella pneumonia , Staphylococcus aureus and Bacillus cereus . The quantitative antimicrobial activity test results proved that all the prepared compounds are very active against Bacillus cereus and that complex very active against Escherichia coli.. Quantum mechanical calculation confirmed the assumption of stability of prepared compounds which agreement with antimicrobial activity results .

INTRODUCTION

Antipyrine and its derivatives have been widely used in different field of medicine over the last few years , the pharmacological and biological activities(1-4) of antipyrine derivatives as well as the antitumour(5,6) , antimicrobial activities(7) are also expected . Therefore with the aim of producing biologically active drugs , the newly synthesized compound (C₁₆H₁₄N₃O₂) and its complex (Cu₂C₃₂H₂₈N₆O₁₂S₂) Were established based on the elemental and spectral analyses which are in good agreement with these structure , Quantum . chemical parameters help to study the geometrical optimization and heat of formation of these compound .

The antimicrobial activity of the antipyrine complexes have been discussed previously(8-15) .

Complex Combinations of copper are used in the treatment of a variety of disease , including inflammatory processes , cancer , ulcers , nervous system and heart diseases further more we have tested the antimicrobial activity of the prepared compound and its complex using strains of Escherichia coli , klebsiella pneumonia staphylococcus aureus and Bacillus cereus .

Experimental Part :

1 – Instruments used :

Infra – red spectrophotometer (pye – Unicam model sp- 3 - 300 S)

CHN analysis (Carlo Erba EA 1108 elemental analyzer)

2 – Synthesis of (C₁₆H₁₄N₃O₂) Compound(15):

A solution of 4 – amino antipyrin (1.25m mol) in methanol (15 ml) was added to a solution of terephthalic aldehyde (0.5m mol)in methanol(15ml) the resulting yellow solution was refluxed for (30 minutes) and then left at room temperature for(6 hrs).The intense yellow precipitate formed was filtered , washed with methanol and dried .

3 – Synthesis of (Cu₂ C₃₂ H₂₈ N₆ O₁₂ S₂) Complex(13) : -

A DMF solution (15 ml) (C₁₆ H₁₄ N₃ O₂) (0.5 m mol) was added to aqueous copper sulphate (1 m mol) dissolved in distiller water (15ml) the resulting green solution was refluxed for (2 hours) . this solution was left at room temperature for (4 days) . A brown precipitate was formed which was filtered,washed with ethanol and dried .

4 – Quantum – mechanical calculations :

For quantum–chemical calculations we have used two important programs Alchemy 2000 and Hyperchem (MNDO semiempirical method) wich were used for geometrical optimization and heat of formation calculation of investigated compounds .

5 – Biological assay : -

The fresh cultures obtained from clinical isolates were suspended in distilled water and adjusted to a standard density of (0.5 macfarland) .

The microbial suspensions were plated on solid Mueller hinton medium and solutions of the test compounds (10 µL) prepared in DMF(1 mg /ml) were added on filter paper disks concomitantly , these disks were impregnated with the same concentration of gentamycin , which was used as reference standard for reporting the antibiotic sensitivity . The plates were incubated at (37°C) for (24 hrs) . The quantitative antimicrobial activity assays were performed by the two - fold serial microdilution method in liquid solution of test compound medium (nutrient broth)(8) .

Serial two – fold dilutions of a solution of test compound in DMF from (1000 to 62.5µg/ml) in a total volume of (200 µl) medium and standard microbial suspension (50 µl) was added in each well. After (18-24hours) The plates are examined visually for evidence of bacterial growth .

RESULTS AND DISCUSSION

1 – infra – red spectra

IR spectra were recorded by using KBr disc were shown in table (1). IR

Spectra of (C₁₆H₁₄N₃O₂) compound was observed that the frequency of the specific band of the (V_{C=N}) bond (1654 cm⁻¹) is moved towards lower wavenumbers by approx. (15 cm⁻¹) in the spectra of the complex (Cu₂ C₃₂ H₂₈ N₆ O₁₂ S₂) which confirms the coordination of the nitrogen atom to the metallic ion. The specific (V_{>C=O}) bond (1595cm⁻¹) of ligand moves towards lower wave number (1565 cm⁻¹) of complex , suggesting the coordination of the ligand to the metallic ion via the (>C=O) group . In complex a characteristic band corresponding to the bidentate coordination of the (So₄²⁻) ion appears . Thus the (V₁)and(V₂) frequencies specific to a (T_d) arrangement appear as medium intensity bands , (V₃) and (V₄) frequencies each split in to three bands , which suggest a low symmetry(16) in complex the (Cu²⁺) ion has a deformed tetrahedral geometry (17) .

2 – Elemental analysis :

The percentage of carbon, hydrogen and nitrogen of prepared compounds are shown in table (2) , the elemental analysis results of prepared compounds are in a good agreement with the calculated values

Tabl (1) : IR spectral data for the prepared ligand and complexe

			Vso42-			
compound	Vc=N	V>C=O	V1	V2	V3	V4
C16H14N3O2	1654	1595				
					1050	574
Cu2 C32 H28 N6 O12 S2	1639	1565	995	462	1105	610
					1170	641

Table (2) : (CHN) analysis of ligand and complex

compound	Practical values				Theoretical values			
	C%	H%	N%	Cu%	C%	H%	N%	Cu%
C16H14N3O2	70.58	6.28	16.2		68.5	5.00	15.0	
			1		7		0	
Cu2 C32 H28 N6 O12 S2	46.12	3.31	9.32	14.09	43.6	3.18	9.55	14.44
					7			

3- Antimicrobial activity assays : -

The antimicrobial activity assays of the (C16 H14 N3 O2) and (Cu2 C32 H28 N6 O12 S2) were performed by quantitative methods based on serial two–fold dilutions of the test compounds in order to establish the corresponding minimal inhibitory concentrations(MIC)at the highest dilution(lowest concentration) of the tested compound

that completely inhibited microbial growth four bacterial strains(*Escherichia coli* , *Klebsiella pneumonia* , *staphylococcus aureus* and *Bacillus cereus*) were cultivated on solid media and incubated at (37°C) for (24 hrs) prior to testing .The quantitative assay results (Figure -1-) showed that the tested compounds exhibited variable (MICs) and selective antimicrobial activity depending on the microbial strains . All tested compounds proved to be active on *Bacillus cereus* well known for its high constitutive and acquired resistance rates and($\text{Cu}_2\text{C}_{32}\text{H}_{28}\text{N}_6\text{O}_{12}\text{S}_2$) complex showed good activity against *E.coli* proving their potential usefulness as broad spectrum antimicrobial agents.

4 – Quantum mechanical results :-

Quantum mechanical calculation of heat of formation (H_f) for ligand and its complex which were prepared in this work has been shown in table (3)

Table (3): Heat of formation (H_f) of ligand and complex

Compound	H_f (kcal / mol)
C₁₆H₁₄N₃O₂	197.45
Cu₂C₃₂H₂₈N₆O₁₂S₂	175.06

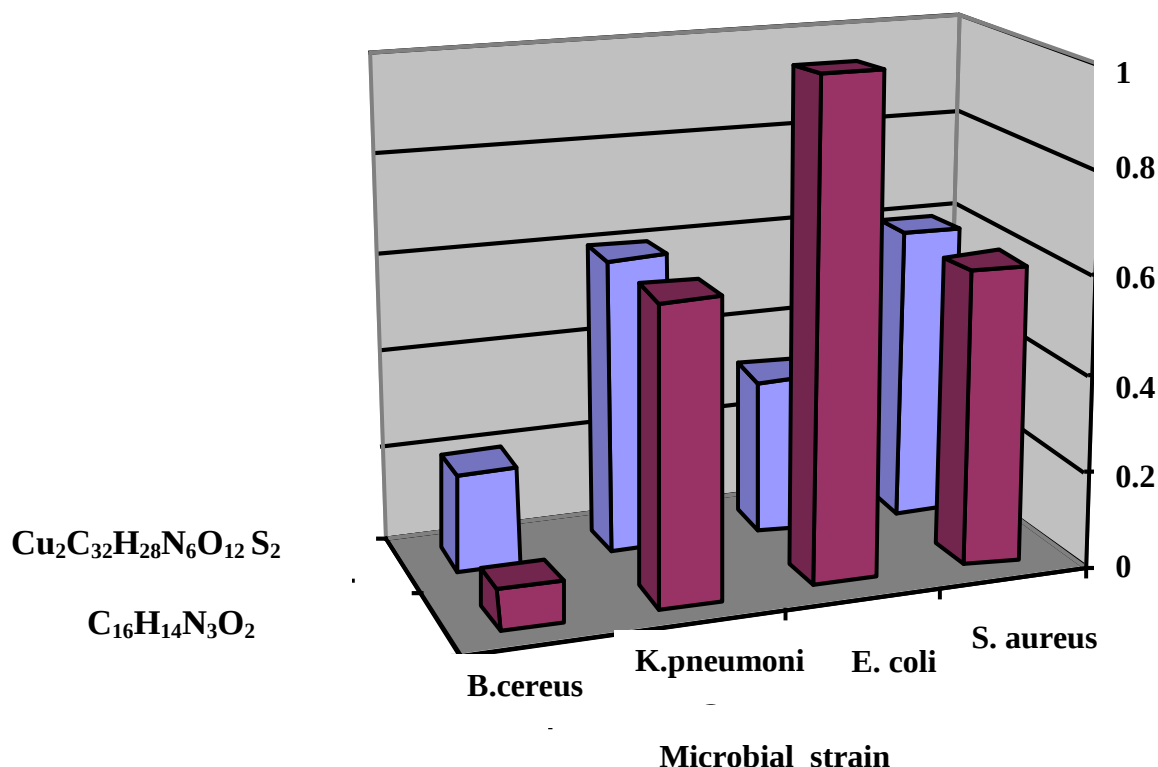


Figure 1: The graphic representation of the MIC values (mg / ml) of the tested compounds towards different bacterial strains

CONCLUSION

- 1 – The IR spectral and (CHN) analysis results indicate that the structure of prepared compounds are as expected .
- 2 – The quantitative anti – microbial activity test results proved that both the ligand and their complex have specific anti – microbial activity depending on the microbial species tested .
- 3 – Heat of formation results proved that the ligand stability increases when its coordinated with (Cu^{2+}) ion therefore its has a great covalency and prevent it from decomposition when it penetrate the cell well then these are agreement with anti – microbial activity test results which its increases when ligand compound are coordinated with (Cu^{2+}) ion .

تحضير ودراسة الخواص الميكانيكية والفعالية البايولوجية لمشتقات جديدة للانتي بايرون

ابتهال حنظل التميمي ، رواء محمد

كلية الصيدلة – جامعة البصرة – البصرة – العراق

الخلاصة

أهتمت الدراسة في هذا البحث تحضير الليكاند ($C_{16}H_{14}N_3O_2$) والمعدن ($O_{12}S_2$) ($Cu_2C_{32}H_{28}N_6$) وقد شخّصت بطريقة تحليل العناصر والمطيافيه وعند دراسة الفعالية البايولوجية ضد أربعة أنواع من البكتيريا أظهرت النتائج أن جميع المركبات المحضرة لها فعالية ضد بكتيريا *B.cereus* وان المعدن الناتج من اتحاد الليكاند مع (Cu^{2+}) أظهر فعالية ضد بكتيريا (*E.coli*) ايضا وان المعالجة الكمية للمركبات المحضرة في هذه الدراسة بينت إن أستقرارية المعدن أعلى من الليكاند وهذا يتوافق مع نتائج دراسة الفعالية البايولوجية ضد البكتيريا لهذه المركبات

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