

**Kurdistan Regional Government- Iraq**  
**Ministry of Higher Education & Scientific Research**  
**Salahaddin University–Erbil (SUE)**  
**College of Science**  
**Department of Chemistry**



## **Acetamide Transition Metal Complexes**

A Project Submitted to the Scientific Committee in The Chemistry Department in Partial Fulfillment of the Requirement for the Degree of B.A or BCs. In Chemistry science.

Prepared by:

Savan Kamaran Ali

Supervised by:

Mr.Muhammad Haji

## List of Contain:

No	Name of Subjects	Page
1	Introduction	1
2	Preparation of [2-chloro-N-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4ylacarbomothioyl)acetamide] (L)	2
3	Electronic Spectra	3
4	Micro elemental analysis and conductance measurements	5
5	Infrared spectra	5
6	Electronic spectra	6
7	In vitro antibacterial and antifungal assay	8
8	Discussion	13
9	Antibacterial Activity	15
10	In-vitro bioactivity test for immunomodulatory and cytotoxicity assessment Separation of human peripheral blood mononuclear cells	17
11	Anticancer screening	17
12	Molar Conductivity (AMP)	21
13	Material and Method	22
14	Preparation of N-(1-Morpholino (3-methoxy, 4hydroxy) benzyl]acetamide (MBA)	22
15	Molar Conductance	24
16	Electronic Spectra	25
17	Antimicrobial studies	29
18	Electronic Absorption Spectra	29
19	Reference	33

## List of Figure:

No of fig.	Name of fig.	Page
1	synthesis of ligand(L)	1
2	N-[Morpholino(phenyl)methyl]acetamide	2
3	A.SO <sub>4</sub> .MBA.2H <sub>2</sub> O (A=Cu )	2
4	A.(NO <sub>3</sub> ) <sub>2</sub> .MBA (A= Co, Ni and Cu).	2
5	CoSO <sub>4</sub> .2MBA	2
6	(a) Proposed structure for S.TH - Ag complex, and (b) Proposed structure for the remaining metal complexes	4
7	DPAMAce	4
8	Ce(SO <sub>4</sub> ) <sub>2</sub> DPAMAce	6
9	Th(NO <sub>3</sub> ) <sub>4</sub> DPAMAce	6
10	UO <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> DPAMAce	6
11	Synthesis the ligand (AMP)	7
12	N[(Diphenylamino)methyl] Acetamide	11
13	ZnSO <sub>4</sub> .DPAMAce.2H <sub>2</sub> O	11
14	CdSO <sub>4</sub> .DPAMAce.2H <sub>2</sub> O	11
15	HgCl <sub>2</sub> .DPAMAce.2H <sub>2</sub> O	11
16	U.V. spectrum of complexe [Hg(L) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ]Cl <sub>2</sub>	15
17	Condensation reaction between 2-thiophenecarboxyaldehyde and sulfacetamide give (E)-N-(4-(thiophen-2-ylmethyleneamino) phenylsulfony) acetamide S. TH.	16
18	The probable structure for Co (II), Cu(II), Th(IV) and Zr(IV) metal complexes.	20
19	Preparation of ligand (MBA)	23
20	A proposed structure of Al(III) cvomplex	27
21	FTIR spectrum of free Paracetamol	27
22	FTIR spectrum of Al(III)- Paracetamol complex	27
23	Synthesis of Schiff base (N-[4-(Phenyliminomethyl)phenyl]acetamide) 0.67 Hydrate	28
24	The structural formulas of the complexes [M(L1) <sub>2</sub> (L2)]Cl <sub>2</sub> and [M(L1) <sub>2</sub> (L3)]Cl <sub>2</sub> , M=Cu(II) or Zn (II)	30
25	Chemical structures of acetaminophen	31
26	N-[Phenyl(pyrrolidin-1-yl)methyl]acetamide(PBA)	32
27	Nickel(II)-CHMAA	32
28	Cobalt(II)-CHMAA	32

## List of Table:

No of table	Name of Table	Page
1	Analytical data of CeIV, ThIV and UIV Complexes of DPAMAce.	
2	Some physical properties of the ligand (L) and its complexes.	
3	The peaks electronic transitions and geometries of the ligand (L) and its properties .	
4	In-vitro bioactivity test for immunomodulatory and cytotoxicity assessment (MTT method).	18
5	Anticancer activities against Raji and Jukart Cell Lines(MTT Method) .	18
6	The analytical and physical data of the compounds	19
7	Some of properties of the ligand(AMP) and their metal complexes.	21
8	Physical characterization, Analytical, Molar conductance Magnetic susceptibility data.	24
9	Elemental analytical data of Schiff base and the metal complexes.	25

## Introduction:

A new ligand [ 2-chloro-N- (1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro -1H-pyrazol- 4ylcarbamothioyl)acetamide](L) was synthesized by reacting the Chloro acetyl isothiocyanate with 4-aminoantipyrene, The ligand was characterized by (C HNS) elemental microanalysis and the spectral measurements including Uv-Vis ,IR ,<sup>1</sup>H and <sup>13</sup>C NMR spectra, some transition metals complex of this ligand were prepared and characterized by Uv-Vis, FT-IR spectra, conductivity measurements, magnetic susceptibility and atomic absorption. From the obtained results the molecular formula of all prepared complexes were [M(L)<sub>2</sub>(H<sub>2</sub>O)<sub>2</sub>]Cl<sub>2</sub> (M+2 =Mn, Co, Ni, Cu, Zn, Cd and Hg), the proposed geometrical structure for all complexes were octahedral (Basima M. Sarhan and Enass J. Waheed et al, 2016 )

## Preparation of [2-chloro-N-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4ylcarbamothioyl)acetamide] (L)

(5.33g, 1mmol) of 4-aminoantipyrene in (20 mL) acetone was rapidly added to Chloro acetyl isothiocyanate and maintaining reflux. After refluxing for 6 hrs, the resulting solid was collected, washed with acetone and recrystallization from ethanol, yield (75%), (m.p =210-212)°C, C% found (50.1) calc.(49.63), H% found (4.75) calc.(4.46), N% found (16.32) calc.(16.54 ), S% found (10.1) calc.(9.46). (Basima M. Sarhan and Enass J. Waheed et al, 2016)

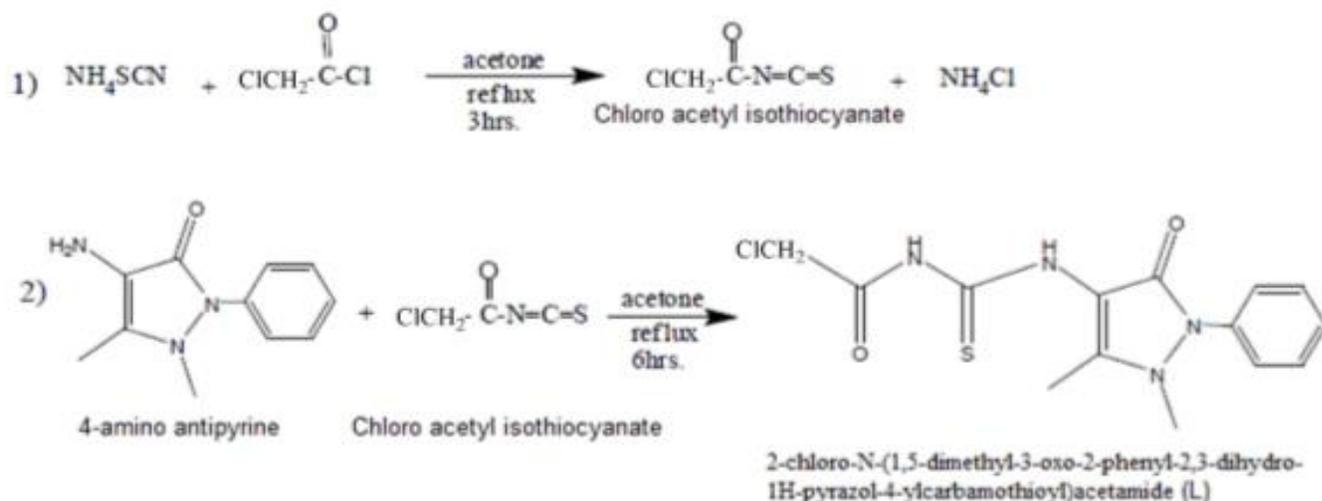


Figure1: synthesis of ligand(L)

A new Mannich base N-[morpholino(phenyl)methyl]acetamide (MBA), was synthesized and characterized by spectral studies. Chelates of MBA with cobalt(II), nickel(II) and copper(II) ions were prepared and characterized by elemental analyses, IR and UV spectral studies. MBA was found to act as a bidentate ligand, bonding through the carbonyl oxygen of acetamide group and CNC nitrogen of morpholine moiety in all the complexes. Based on the magnetic moment values and UV-Visible spectral data, tetra-coordinate geometry for nitrate complexes and hexacoordinate geometry for sulphato complexes were assigned. The antimicrobial studies show that the Co(II) nitrate complex is more active than the other complexes. ( L.MURUGANANDAM and K.KRISHNAKUMAR, 2011 )

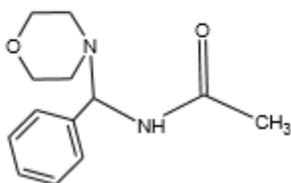


Figure2: N-[Morpholino(phenyl)methyl] acetamide.

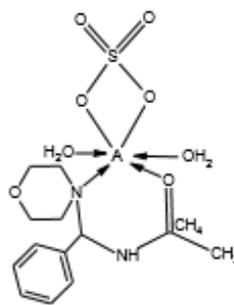


Figure3: A.SO4.MBA.2H2O (A=Cu ).

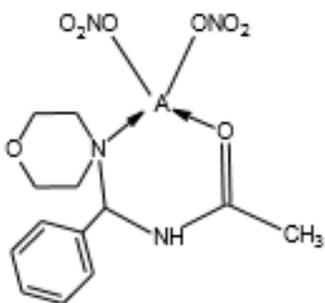


Figure4: A.(NO3)2.MBA (A= Co, Ni and Cu).

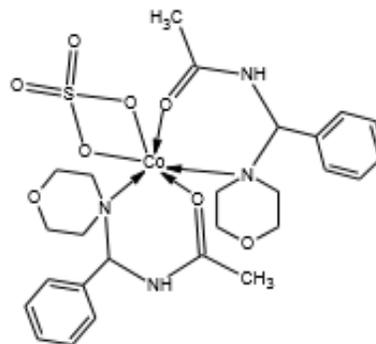


Figure5: CoSO4.2MBA

The synthesized compositions have been characterized using different physico-chemical techniques. The investigation included elemental analysis, melting point measurements, proton NMR, UV spectroscopy, FT-IR, magnetic susceptibility, conductance measurements, mass spectral analysis, and inductively coupled plasma mass spectrometry (ICP-MS) for determining the concentrations of metal ions. The measured values for molar conductance indicated that the majority of the prepared complexes were nonelectrolytes. The biological activity of the prepared compositions has been investigated. (Ahmad S. Abu-Khadra and Ahmad S. Afify et al, 2018)

## Electronic Spectra

Electronic spectra of complexes can provide valuable information related to stereochemistry of metal ions in the complexes based on the positions and number of d-d transition peaks. The electronic spectra for all compounds were obtained in DMSO solution and show absorption bands in three distinct regions. The first region ranging from 200 to approximately 249 nm, is characteristic for the electronic inter-ligand  $\pi \rightarrow \pi^*$  transitions correspond to transition C=C of the phenyl group, while the second characteristic wavelength in the region of 280 nm to approximately 350 nm is the second inter ligand  $n \rightarrow \pi$  transition C=O, the third distinct region ranging from 410 nm to approximately 540 nm is an indicator for the Ligand to Metal Charge Transfer (LMCT) from the nitrogen atom to the transition metal center [22 - 24]. The UV bands of SO<sub>2</sub> group merge to form a single strong absorption band around 260 nm. Many bands positions are considerably shifted from their original positions in their ligands to blue or red regions in all complexes indicating coordination to the metal, while new bands were observed in the visible region for the complexes due to d-d transitions. In case of a d<sup>10</sup> system (Ag & Zn complexes) the present diamagnetic complexes show no d-d transition in the visible region. (Ahmad S. Abu-Khadra and Ahmad S. Afify et a, 2018l)

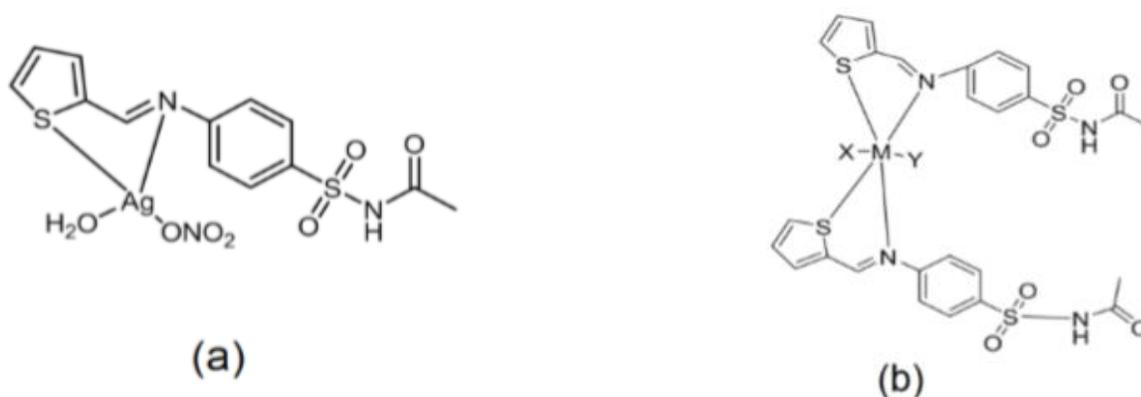


Figure6: (a) Proposed structure for S.TH - Ag complex, and (b) Proposed structure for the remaining metal complexes

N-[(Diphenylamino)methyl]acetamide was synthesized using Mannich reaction and its complexes of cerium(IV), thorium(IV) and dioxouranium(VI) were prepared and characterized by elemental analysis and various spectral studies. The bidentate chelation of ligand, bonding through carbonyl oxygen and azomethine nitrogen is suggested. Based on spectral and magnetic studies, hexa coordinate geometry is assigned for all the complexes. The complexes were screened for their antibacterial, antifungal and anticancer activities. They show positive results. (L. MURUGANANDAM and K. KRISKNA KUMAR et al, 2012)

The mass spectrum 11 of the ligand exhibits a molecular ion peak at  $m/z = 252$ , which corresponds to the imposed molecular mass of the compound. Based on the data obtained from various physical and chemical studies, the molecular structure of DPAMAce is shown in Figure7. (L. MURUGANANDAM and K. KRISKNA KUMAR et al, 2012)

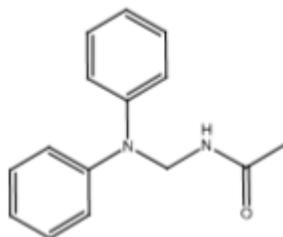


Figure7: DPAMAce

## Micro elemental analysis and conductance measurements

The  $\Lambda m$  values for  $10^{-3}$  M DMF solutions of all the complexes suggest that, they are nonelectrolytes. The analytical data for C, H, N, metal and anion content in the complexes are given in Table1. (L. MURUGANANDAM and K. KRISKNA KUMAR et al, 2012)

**Table 1.** Analytical data of  $Ce^{IV}$ ,  $Th^{IV}$  and  $U^{VI}$  Complexes of DPAMAc

Complex	% C	% H	% N	%Metal	%Anion	$\Lambda m \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$
	Obs. (Cal.)	Obs. (Cal.)	Obs. (Cal.)	Obs. (Cal.)	Obs. (Cal.)	
L	73.01 (75.00)	6.19 (6.60)	11.58 (11.60)	-	-	-
$Ce(SO_4)_2 \cdot L$	38.02 (37.80)	3.19 (3.36)	6.05 (5.88)	30.21 (29.43)	19.71 (20.17)	14.52
$Th(NO_3)_4 \cdot L$	25.10 (24.99)	2.64 (2.22)	11.13 (11.66)	32.83 (32.26)	34.09 (34.43)	09.86
$UO_2(NO_3)_2 \cdot L$	28.76 (28.37)	2.90 (2.52)	8.06 (8.83)	37.47 (37.54)	20.21 (19.16)	17.03

## Infrared spectra

Comparison of the IR spectrum of ligand with those of its complexes suggests the following: Perceptible shifts by about 32 to 40 and 65 to 108  $cm^{-1}$  are observed in the  $\nu_{CO}$  and  $\nu_{CNC}$  respectively in the case of cerium(IV) sulphato and thorium(IV) & dioxouranium(VI) nitrate complexes. The diagnostic bands of the nitrate group in thorium(IV) and dioxouranium(VI) complexes show a separation of  $(\nu_5-\nu_1)=74 \text{ cm}^{-1}$  which indicates the monodentate mode of coordination. The band at 582  $cm^{-1}$  represents the formation of  $\nu_{Th-N}$  bond<sup>9</sup> in the thorium(IV) complex.. The new bands formed at 506 & 472  $cm^{-1}$  indicates the presence of  $\nu_{Th-O}$  bond. The bands at 914 & 940  $cm^{-1}$  are evidences for O=U=O bond. The medium bands found at 500– 584  $cm^{-1}$  are assigned to  $\nu_{M-N}$  and  $\nu_{M-O}$  vibrations in uranium(VI) complex. The cerium(IV) sulphato complex registers new strong bands in the range of 1108, 996, 914( $\nu_3$ ), 877( $\nu_1$ ), 693, 654, 609( $\nu_4$ ), 502  $cm^{-1}$  ( $\nu_2$ ) which point to a bidentate coordination of the sulphato group. (L. MURUGANANDAM and K. KRISKNA KUMAR et al, 2012)

## Electronic spectra

In Ce(IV) sulphato complex, a broad band observed at  $27800\text{ cm}^{-1}$  is due to charge transfer transition. The magnetic moment of this complex: 2.57 B.M., which indicates the absence of metal-metal interaction and spin exchange. There is no characteristic intense band in the visible region for Th(IV) nitrate complex, since it is a  $d^{10}$  system. The electronic spectrum of dioxouranium(VI) nitrate complex exhibits a band at  $21934\text{ cm}^{-1}$  assignable to the  $1_{Eg} \rightarrow 3_{\Pi u}$  transition. Also the presence of a band at  $18579\text{ cm}^{-1}$  suggests that the uranyl ion is surrounded by four equatorial groups. The complex exhibits a magnetic moment of 0.12 B.M, suggesting the six coordinated geometry. (L. MURUGANANDAM and K. KRISKNA KUMAR et al, 2012)

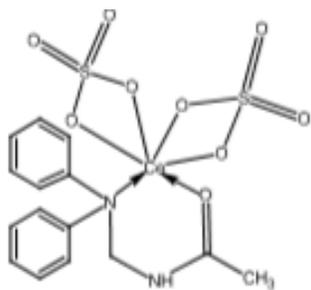


Figure8:  $\text{Ce}(\text{SO}_4)_2$   
DPAMAce

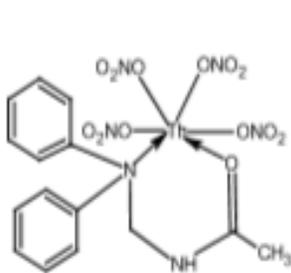


Figure9:  $\text{Th}(\text{NO}_3)_4$   
DPAMAce

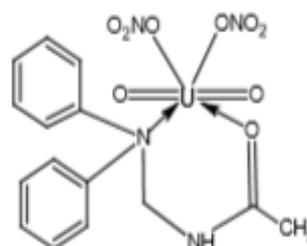


Figure10:  $\text{UO}_2(\text{NO}_3)_2$   
DPAMAce

The new bidentate Schiff base ligand (E)-N-(4-hydroxy-3-(1-(2-isonicotinoylhydrazono)ethyl)phenyl)acetamide (LH) and its Cu(II), Co(II), Th(IV) and Zr(IV) complexes have been synthesized by the conventional method. Compounds have been characterized by elemental analysis, IR, FAB-Mass, molar conductivities, magnetic measurements, electronic spectra, ESR and thermal analysis. Analytical data suggested 1:2 (metal: ligand) mole ratio for all the complexes. The low molar conductance values of the metal complexes in DMSO reveal their non-electrolytic nature. From the observed data of magnetic moment and electronic spectra, the six coordinated structures for all the complexes, have been proposed. The thermodynamic analysis shows that the complexes lose hydrated and/or coordinated water molecules in the first step; followed by decomposition of ligand moiety in the further steps leading to formation of stable oxide. The

antibacterial screening results also indicate that the metal complexes are good antibacterial agents as compared to the Schiff base. (Prashant R. Mandlik and Partik K. Deshmukh, 2020)

A new ligand N-(methylcarbamothioyl) acetamide (AMP) was synthesized by reaction of acetyl chloride with adenine. The ligand was characterized by FT-IR, NMR spectra and the elemental analysis. The transition metal complexes of this ligand were synthesized and characterized by UV-Visible spectra, FT-IR, magnetic susceptibility, conductivity measurement. The general formula  $[M(AMP)_2Cl_2]$ , where  $M^{+2} = (Mn, Co, Ni, Cu, Zn, Cd, Hg)$ . (Hiba A. Ghani and Basima M. Sarhan, 2020)

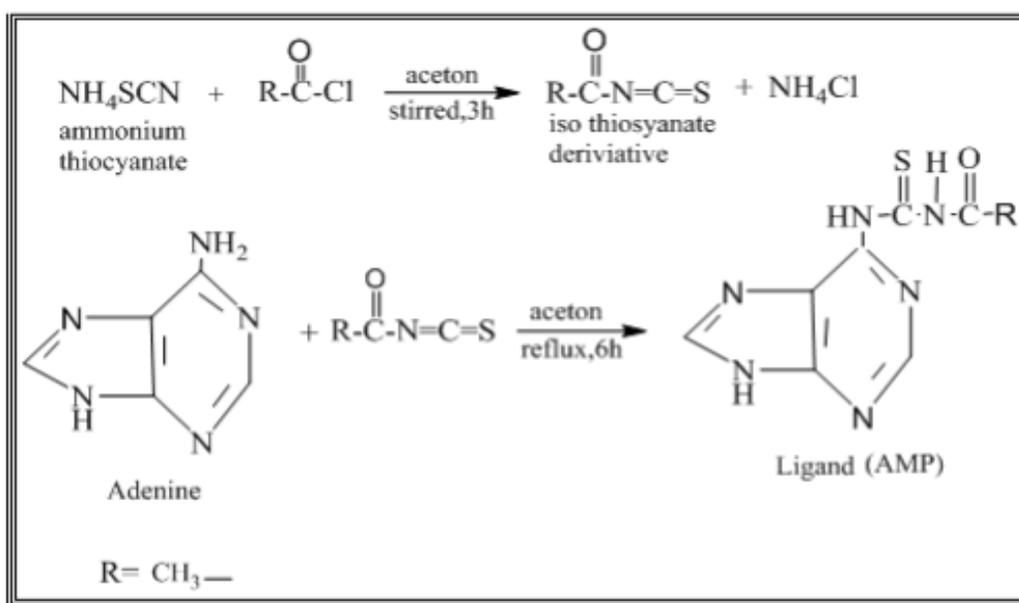


Figure 11: Synthesis the ligand (AMP)

The synthesis of a new series of complexes of Fe(II), Co(II), Ni(II) and Cu (II) ions with mixed Ligand involved Mannich Ligand (L) and diamine ligand (L'). L Ligands involved L<sub>1</sub>, L<sub>2</sub>, L<sub>3</sub> namely L<sub>1</sub>=N-[1-Morpholino(3-methoxy,4-hydroxy) Benzyl] Acetamide (MBA), L<sub>2</sub>=N-[1-Morpholino(3-methoxy, 4-hydroxy) Benzyl] benzamide (MBB), L<sub>3</sub>= N-[1-Morpholino(3-methoxy,4-hydroxy( Benzyl] urea (MBU). L' ligand is 1,10-phenanthroline. These complexes were prepared from the direct reaction of the metal(II) chloride, mannich bases (MBA, MBB, MBU) and

diamine ligand namely with mole ratio of (1:1:2) of L:M:L' Categories of complexes were synthesis is mononuclear complexes of formula  $[M(L)(L')]Cl_2$  where: M= Fe(II), Co(II), Ni(II), Cu(II), L= mannich base MBA, MBB, MBU, L'=1-10 phenanthroline. These complexes were characterized on bases of their physical properties and spectroscopic data such as melting points, molar conductivity, elemental analysis (C.H.N) and atomic absorption techniques as well as spectral studies such as UV-Vis, IR, magnetic susceptibility also have been measured The completion of the reaction checked by using TLC. From all data all complexes exhibit octahedral geometry. (Amaaly Al-Assafe and Bara S. Dobany, 2019)

Novel Mannich base derivatives of acetamide were prepared through three-component condensation reaction. The present study deals with the structure and antimicrobial properties of some complexes of Mn(II), Co(II), Ni(II) and Zn(II) with a new Mannich base N-(3-(furan-2-yl)-3-oxo-1-phenylpropyl)acetamide. All the compounds were characterized through spectral and analytical data. The transition metal complexes of resultant Mannich bases have been synthesized and well characterized by elemental analyses, spectral studies, magnetic moment determination, molar conductivity measurement and thermogravimetric analysis. Experimental results showed that metal complexes act as bidentate ligands. The in-vitro antibacterial and antifungal activity of Mannich bases and their metal (II) complexes was assayed against different pathogens using MIC method. All the compounds and their metal complexes showed good potency against various microorganisms. (U. Rizwan Sulthana and M.Shanamuga priya et al, 2018)

### **In vitro antibacterial and antifungal assay**

The biological activities of synthesized Mannich base and its Mn(II), Co(II), Ni(II) and Zn(II) complexes have been studied for their antibacterial and antifungal activities by Disc diffusion test using Nutrient agar (NA) and Sabouraud Dextrose Agar(SDA). The antibacterial and antifungal activities were done at 10 µg/mL concentrations in DMSO solvent using bacteria (*S aureus*, *B substillis*, *E.coli* and *P.aeruginosa*) and fungi(*C.albicans*, *A.niger*) at the minimum inhibitory concentration (MIC) method. These bacterial strains were incubated for 24 h at 37 °C and fungi strains were incubated for 48 h at 37 °C. Standard antibacterial (ciprofloxacin) and antifungal drug (Nystatin) were used for comparison under

similar conditions. Activity was determined by measuring the diameter of the zone showing complete inhibition (mm). (U. Rizwan Sulthana and M. Shanamuga priya et al, 2018)

A newly synthesized Schiff bases N-bis-(salicylidene)-2-4-diamino-5-chlorothiazole and N-bis-(5methylsalicylidene)-2-4 diamino-5-chloro-thiazole and metal ion CoII, NiII, CuII and ZnII, their metal complexes have been reported. The complexes are characterized by elemental analysis, UV-visible and infrared spectra, magnetic susceptibility and conductivity measurement. The Schiff base act as monomeric as well as dimeric to CoII, CuII and NiII, ZnII respectively. The ligand coordinate through oxygen atom of phenolic OH group and the nitrogen atom of azomethine group. The complexes are nonelectrolytic in nature. The Schiff bases and their metal complexes were screened for antibacterial fungicidal and pesticidal activity. (BN Muthal and BN Raut, 2015)

The complex of Al (111) with paracetamol have synthesized and characterized using UV-Vis, Infrared spectroscopies and melting point. The ligand has been found to behave as tridentate chelating agents. Paracetamol complex coordinate through the carboxylate oxygen, phenolate oxygen atom, and amine group. The complex solubility was evaluated for several solvents and it was found the compound was more soluble in DMSO. Job's method of continuous variation suggested 1 : 2 metals to ligand stoichiometry for paracetamol complex. ((Mohand A. Sultan and Ali E. Karim et al, 2020)

The word acetaminophen and paracetamol both originate from a chemical name for the compound Para-acetylaminophenol and para-acetylaminophenol C<sub>8</sub>H<sub>9</sub>NO<sub>2</sub>. Acetaminophen is a white solid which melts at 170<sup>0</sup>C, soluble in water and methanol. Paracetamol is widely used without prescription as a painkiller and fever reducer. Morse first synthesized it in 1878. The discovery of paracetamol was an accident when a patient was given a same molecule (acetamide) roughly 100 years ago. However, acetamide is toxic in a mild quantity. Consequently, scientists started to alter the acetamide's structure to try and to make a new compound that possessed less toxicity but remained the integrity of its structure, and thus Acetaminophen was found. Acetaminophen was prepared by reaction of p-nitrophenol with acetic acid at a free-air environment in the presence of argon atmosphere. Then thermal treatment at 230<sup>0</sup>C was performed, and it was followed by constant stirring for 15 hours. (Mohand A. Sultan and Ali E. Karim et al, 2020)

Four Complexes of thiourea derivative (4-methoxy- N(phenylcarbamothioyl) benzamide) have been prepared by the reaction of 4-methoxybenzoyl isothiocyanate with aniline, then the ligand obtained reacted with ( $Mn^{II}, Co^{II}, Cu^{II}, Ni^{II}$ ) the resulting complexes were characterized by elemental analysis, FTIR, UV-Vis spectra and melting point. General formula that obtained is  $[L_2MCl_2]$  for all complexes with octahedral geometry, where  $(L) = (4\text{-methoxy-N(phenylcarbamothioyl)benzamide})$  and  $M = (Mn^{II}, Co^{II}, Cu^{II}, Ni^{II})$ . (Sallal Abdulhadi AL-Merhj)

The Schiff base (N-[4-(Phenyliminomethyl)phenyl]acetamide 0.67-hydrate) was prepared from 4-acetoamino benzaldehyde and aniline by refluxing the two in ethanolic solution. The metal complexes of Mn (II), Co (II) and Ni (II), were prepared by mixing and refluxing methanolic solutions of  $MnCl_2$ ,  $CoCl_2$  and  $NiCl_2$  with N-[4(Phenyliminomethyl)phenyl]acetamide 0.67-hydrate. Metal Schiff base complexes were prepared and characterized by using different techniques, such as; infrared and atomic absorption spectroscopy. Octahedral geometry was proposed for synthesized metal complexes by comparing theoretical and estimated metal ligand ratio. All the synthesized compounds were tested for their antibacterial activity against *Staphylococcus epidermidis*, *Escherichia coli* and *Staphylococcus aureus* bacteria. Schiff base itself was inactive against these bacteria whereas its complexes with Mn (II), Co (II) and Ni (II) have remarkable action against these bacteria, indicating that they can be used as bactericidal agents. (TARIQ MAHMUD and RABIA REHMAN et al, 2011)

The complexes of  $Zn^{II}$ ,  $Cd^{II}$  and  $Hg^{II}$  with N-[(Diphenylamino)methyl]acetamide (DPAMAce) have been synthesized and characterized. The resulting complexes were characterized by elemental analysis, conductivity measurements, IR and  $^1H$  NMR spectral studies. The Mannich base ligand acts as a neutral bidentate, coordinating through the carbonyl oxygen and azomethine nitrogen atoms. The complexes are non-electrolytic in DMSO. The presence of the coordinated water molecules in all the complexes was indicated by IR spectra of the complexes. From the analytical and spectral data, all the four complexes exhibit octahedral geometry. The antimicrobial activities of ligand and their complexes were screened by disc diffusion method. It is found that the metal complexes have higher antimicrobial activity than the free ligand. (L. Muruganandam and S. Selvam et al, 2015)

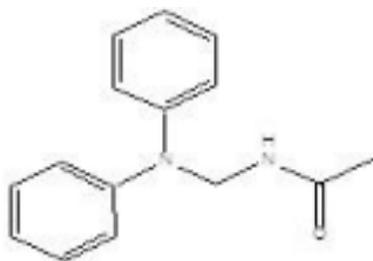


Figure12: N[(Diphenylamino)methyl]  
Acetamide

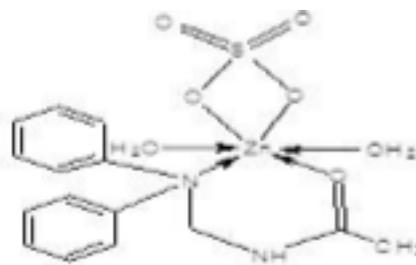


Figure13: ZnSO<sub>4</sub>.DPAMAce.2H<sub>2</sub>O

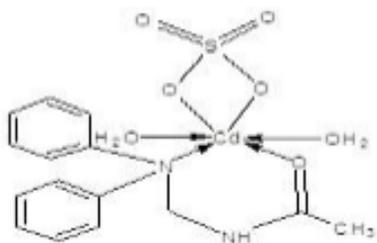


Figure14: CdSO<sub>4</sub>.DPAMAce.2H<sub>2</sub>O

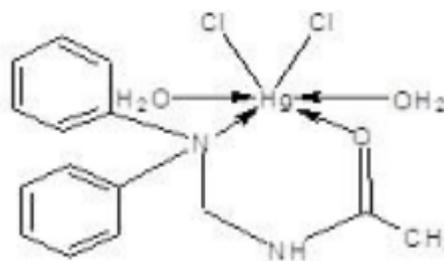


Figure15: HgCl<sub>2</sub>.DPAMAce.2H<sub>2</sub>O

Several mixed ligand Cu(II), Zn(II) complexes using (benzylidenethiourea) (obtained by the condensation of benzaldehyde and thiourea) as the primary ligand and (acetamide or thioacetamide) as an additional ligand were synthesized and characterized analytically and spectroscopically, magnetic susceptibility and molar conductance measurements, as well as by UV-Vis and IR spectroscopy. The interaction of the complexes with calf thymus (CT) DNA was studied using absorption spectra, while the concentration of DNA in gel electrophoresis remained constant at 10  $\mu$ l. They exhibit absorption hypochromicity increased during the binding of the complexes to calf thymus DNA. The complexes show enhanced antimicrobial activities complexes with the free ligand. A theoretical treatment of the formation of complexes in the gas phase was studied. This was done by using the HYPERCHEM-6 program for the Molecular mechanics and Semi-empirical calculations. (Omar H. Al-Obaidi, 2012)

Four new [copper(II) and iron(III)] complexes were synthesized using N-(4-hydroxy-3((piperidin-1-yl)methyl)phenyl)acetamide (HL) a Mannich base as ligand. All compounds were successfully characterized by elemental analysis, conductivity measurements, Ultraviolet-visible, Infrared, and Nuclear Magnetic Resonance spectroscopy. Furthermore, the structural determination of HL by X-ray diffraction technique at room temperature showed that the ligand crystallized in the monoclinic crystal system with space group Cc and Z=4. Structural analysis revealed the chelation of the ligand and the bonding mode of the thiocyanate group. All the metal complexes demonstrated considerable abilities to oxidize 3, 5-di-tert-butylcatechol in DMF under aerobic conditions. Complex 3 (with an iron(III) center) displayed the highest turnover rate of  $14.69 \pm 0.71 \text{ h}^{-1}$ . (AYOWOLE O. AYENI and GARETH M. WATKINS,2020)

Mixed ligand complexes derived from diclofenac potassium salt (Kdc) and acetaminophen (ace) has been synthesized and proposed to have a general formula [MB] where  $M = \text{Co}^{2+}, \text{Ni}^{2+}, \text{Cu}^{2+}$  and  $\text{Zn}^{2+}$  and  $B = (\text{ace})(\text{dc})(\text{H}_2\text{O})_2$  except for  $\text{Mn}^{2+}$  complex which exists as  $[\text{Mn}(\text{ace})(\text{dc})\text{OH}_2]$ . The complexes were characterized by solubility, melting point, conductivity, elemental analyses, UV-Vis, FT-IR spectroscopy, X-ray powder diffraction (XRPD) study and magnetic susceptibility measurement. Electronic absorption spectra data are characteristic of octahedral structures for [MB]. The IR spectra revealed a bidentate coordination mode. In acetaminophen, the nitrogen and carbonyl-O atoms of the amide group were involved while the carboxylate oxygen atoms of potassium diclofenac were used; typical of a carboxylic acid derivative. The compounds were screened for in-vitro anti-inflammatory activity by inhibition of albumin denaturation assay and antimicrobial activity against bacteria strains: *Bacillus subtilis*, *Bacillus anthrax*, *Escherichia coli*, *Salmonella typhi* and a fungus *Aspergillus niger*. Some of the tested compounds showed moderate anti-inflammatory activity when compared to the standard drug diclofenac potassium salt. The in-vitro antimicrobial screening revealed an increased activity of the complexes against the bacteria isolates compared to the free ligands. (J.A. Obaleye and A.A. Aliyu et al,2021)

A new Mannich base ligand: N-[Phenyl(pyrrolidin-1yl)methyl]acetamide(PBA) was prepared and characterized by elemental analysis and various spectral studies. Some

metal complexes of a ligand with  $\text{Co}^{\text{II}}$ ,  $\text{Ni}^{\text{II}}$  and  $\text{Cu}^{\text{II}}$  have been synthesized and characterized by elemental analysis, molar conductance values, magnetic susceptibility measurements and various spectral studies. The spectral data reveals that the ligand acts as bidentate and tridentate coordination to the metal ion through the CNC nitrogen, carbonyl oxygen and amido nitrogen atoms. Based on the magnetic and electronic studies, all the complexes are high spin octahedral geometry. The conductance measurements indicate that the non-electrolytic nature of the complexes. The biological activities of the ligand and complexes have been screened in vitro against some bacteria and pathogenic fungi to study their capacity to inhibit their growth. (L. Muruganandam and S. Slevam, 2017)

## **Discussion:**

In recent years, there has been increasing interest in synthesis of heterocyclic compounds that have biological and commercial importance. Antipyrine compounds play an important role in modern organic synthesis, not only because they constitute a particularly useful class of heterocyclic compounds, but also because they are of great biological interest. One of the most important derivatives of antipyrine is 4-aminoantipyrine, It is very important in the field of Medicinal and Agricultural chemistry. It is also used as a hemolytic inhibitors, polarographic titration, conductometric and potentiometric determination of lanthanides. 4-aminoantipyrine have large scale of applications in biological, clinical, analgesics, antifungal, antibacterial, anticancerous and pharmacological areas. synthesis a new series of transition metal complexes of Mn(II), Cu(II) from the Schiff base ligand derived from 4-aminoantipyrine, furfural and o-phenylene diamine. synthesis Mn (II), Co (II), Ni (II), Cu (II), Zn(II), Cd (II), Hg(II) and Pb(II) complexes of Schiff base ligand containing 4-aminoantipyrine in a good yield and characterized using IR,  $^1\text{H}$ NMR, UV-Vis., mass spectra, magnetic susceptibility and molar conductivity . A new ligand synthesis by the reaction of 4-aminoantipyrine with 4-dimethylaminobenzaldehyde ,the complexes of Co(II), Zn(II) Cd(II) and Hg(II) with this ligand have been prepared and characterized by elemental analysis, FTIR and Uv-Vis spectra. Anew research using a phosphonium-1-indenylide (PHIN) ligand with 4,7-dimethyl-1-C<sub>9</sub>H<sub>4</sub>PMePh and synthesis of a new PHIN complexes of

rhodium and iridium, The aim of this work is to prepare and characterize a new ligand (Basima M. Sarhan and Enass J. waheed, 2016)

Table2: some physical properties of the ligand (L) and its complexes.

Product	M.wt (gm/mol)	Color	m.p. °C	M% Calculation (Found)	Molar Cond. $\text{Ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$ in DMSO	$\mu_{\text{eff}}$ (B.M)
$\text{C}_{14}\text{H}_{15}\text{N}_4\text{O}_2\text{SCl}$ L	338.81	Brown	210-212	-	1.65	
$[\text{Mn}(\text{L})_2(\text{H}_2\text{O})_2]\text{Cl}_2$	839.56	Brown	234-236	7.00 (6.01)	76	5.93
$[\text{Co}(\text{L})_2(\text{H}_2\text{O})_2]\text{Cl}_2$	843.56	deep violet	231-233	7.51 (7.32)	77.15	4.82
$[\text{Ni}(\text{L})_2(\text{H}_2\text{O})_2]\text{Cl}_2$	843.33	Green	232-234	7.48 (8.11)	74	3.03
$[\text{Cu}(\text{L})_2(\text{H}_2\text{O})_2]\text{Cl}_2$	848.16	Brown	228-230	8.09 (8.60)	69.8	1.72
$[\text{Zn}(\text{L})_2(\text{H}_2\text{O})_2]\text{Cl}_2$	850	Brown	256-258	8.33 (8.15)	81	0
$[\text{Cd}(\text{L})_2(\text{H}_2\text{O})_2]\text{Cl}_2$	897.03	Brown	255-257	14.33 (14.51)	85	0
$[\text{Hg}(\text{L})_2(\text{H}_2\text{O})_2]\text{Cl}_2$	985.21	Brown	227-229	25.57 (26.11)	70	0

Table3: The peaks electronic transitions and structure geometries of the ligand (L) and its complexes.

Compounds	$\lambda(\text{nm})$	$\nu(\text{cm}^{-1})$	ABC	$\epsilon_{\text{max}}$ molar $^{-1} \text{cm}^{-1}$	Transitions
Ligand (L)	297	33670	2.493	2493	$\pi \longrightarrow \pi^*$
$[\text{Mn}(\text{L})_2(\text{H}_2\text{O})_2]\text{Cl}_2$	296 711 930	37174 14064 10752	2.401 0.011 0.013	2401 11 13	LF ${}^6\text{A}_{1g} \longrightarrow {}^4\text{T}_{2g(\text{G})}$ ${}^6\text{A}_{1g} \longrightarrow {}^4\text{T}_{1g(\text{G})}$
$[\text{Co}(\text{L})_2(\text{H}_2\text{O})_2]\text{Cl}_2$	297 360 680 832	33670 27777 14705 12019	2.120 0.332 0.030 0.011	2120 332 30 11	LF C.T mixed with ${}^4\text{T}_{1g(\text{F})} \longrightarrow {}^4\text{T}_{1g(\text{P})}$ ${}^4\text{T}_{1g(\text{F})} \longrightarrow {}^4\text{A}_{2g}$ ${}^4\text{T}_{1g(\text{F})} \longrightarrow {}^4\text{T}_{2g(\text{F})}$
$[\text{Ni}(\text{L})_2(\text{H}_2\text{O})_2]\text{Cl}_2$	257 364 450 796	38910 27472 22222 12562	1.386 1.521 p0.282 0.082	1386 1521 282 82	LF C.T mixed with ${}^3\text{A}_{2g} \longrightarrow {}^3\text{T}_{1g(\text{P})}$ ${}^3\text{A}_{2g} \longrightarrow {}^3\text{T}_{1g(\text{F})}$ ${}^3\text{A}_{2g} \longrightarrow {}^3\text{T}_{2g(\text{F})}$
$[\text{Cu}(\text{L})_2(\text{H}_2\text{O})_2]\text{Cl}_2$	293 848	34129 11792	2.062 0.019	2062 19	C.T ${}^2\text{E}_g \longrightarrow {}^2\text{T}_{2g}$
$[\text{Zn}(\text{L})_2(\text{H}_2\text{O})_2]\text{Cl}_2$	293	34129	2.013	2013	C.T
$[\text{Cd}(\text{L})_2(\text{H}_2\text{O})_2]\text{Cl}_2$	295	33898	2.112	2112	C.T
$[\text{Hg}(\text{L})_2(\text{H}_2\text{O})_2]\text{Cl}_2$	257 364	38910 27472	1.362 1.632	1362 1632	C.T C.T

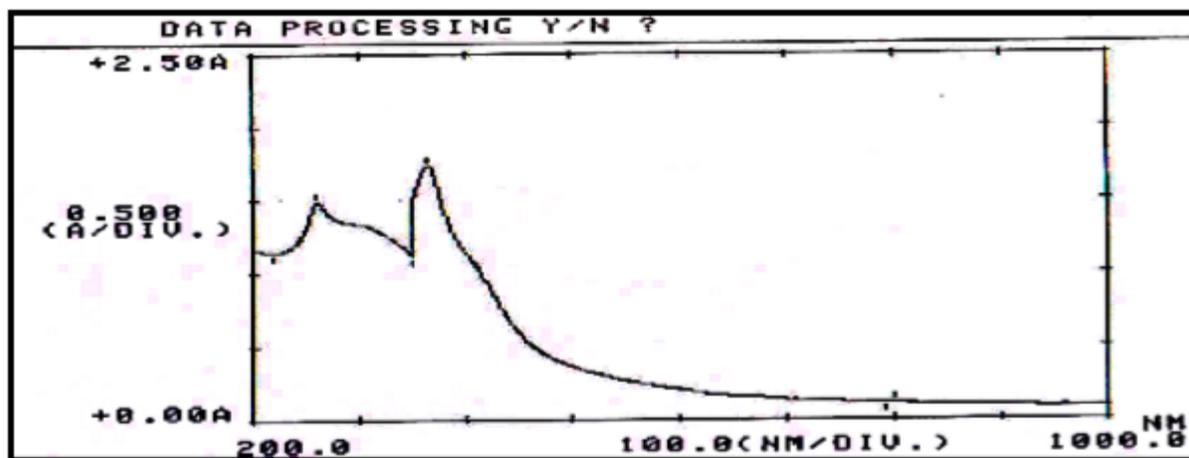


Figure16: U.V. spectrum of complex  $[\text{Hg}(\text{L})_2(\text{H}_2\text{O})_2]\text{Cl}_2$

Metal chelates of Mannich bases form an interesting class of compounds, which find extensive applications in various fields. Among the very few number and variety of transition, inner transition and main group metal complexes of Mannich bases, those formed from bivalent transition metals are of particular interest, because of their synthetic flexibility, structural diversities, bonding interactions, biological significance, and other multiple applications<sup>3-5</sup>. We report here, the synthesis of the Mannich base MBA, which is a bidentate ligand. For, it contains two donor atoms: carbonyl oxygen and CNC nitrogen. With this ligand  $\text{Co}^{\text{II}}$ ,  $\text{Ni}^{\text{II}}$ , and  $\text{Cu}^{\text{II}}$  (in the molar ratio 1:2) complexes have been prepared. (L. MURGANANDAM and K. KRISHNAKUMAR, 2011)

### **Antibacterial Activity**

A comparison of diameters of the inhibition zones of the compounds investigated and listed shows that  $\text{Co}^{\text{II}}$  nitrate complex exhibits highest antibacterial and antifungal activity against all the bacterial and fungal species studied. This is because, they have larger diameters of inhibition zones than even the control gentamycin at the same concentration and identical conditions. The complexes have more antibacterial and antifungal activities than the ligand against all the bacteria and fungi studied. This observation clearly indicates that the chelation increases the activity. The higher activity of the  $\text{Co}^{\text{II}}$  complex may be due to the fact that,  $\text{Co}(\text{II})$  is an essential micronutrient during transcription and transformation of nucleic acids.  $\text{Co}^{\text{II}}$  complexes were shown to inhibit cellular protein and RNA synthesis. In  $\text{Co}^{\text{II}}$  nitrate complex, the unsaturated metal center present, achieves higher coordination

number by binding with some of the functional groups of the protein. This leads to the increased uptake of the compound by the bacterium and thereby inhibiting its growth. Steric constraints are less for a tetrahedral complex than for an octahedral complex. So the tetrahedral complexes are biologically more active than the octahedral complexes. (L. MURGANANDAM and K. KRISHNAKUMAR,2011)

Schiff bases (imines) are the products of condensation of primary amines with carbonyl compounds in acidic medium. Imines were first reported in 1864 by Schiff H. The formation of carbon-nitrogen double bonds is a very important step in organic synthesis due to their significant biological activities such as anticancer, anti-inflammatory and antitumor agents, antibacterial, insecticidal, antimicrobial, anticonvulsant activity, antituberculosis. Additionally, Schiff bases are useful as versatile constituents in nucleophilic addition reactions including organometallic reagents as well as in the reactions including cycloadditions. They have been widely used in dye and food industries, catalytic processes, analytical chemistry, in addition to several agrochemical applications. (Ahmad S. Abu-Khadra and Ahmad S. Afify et al, 2018)

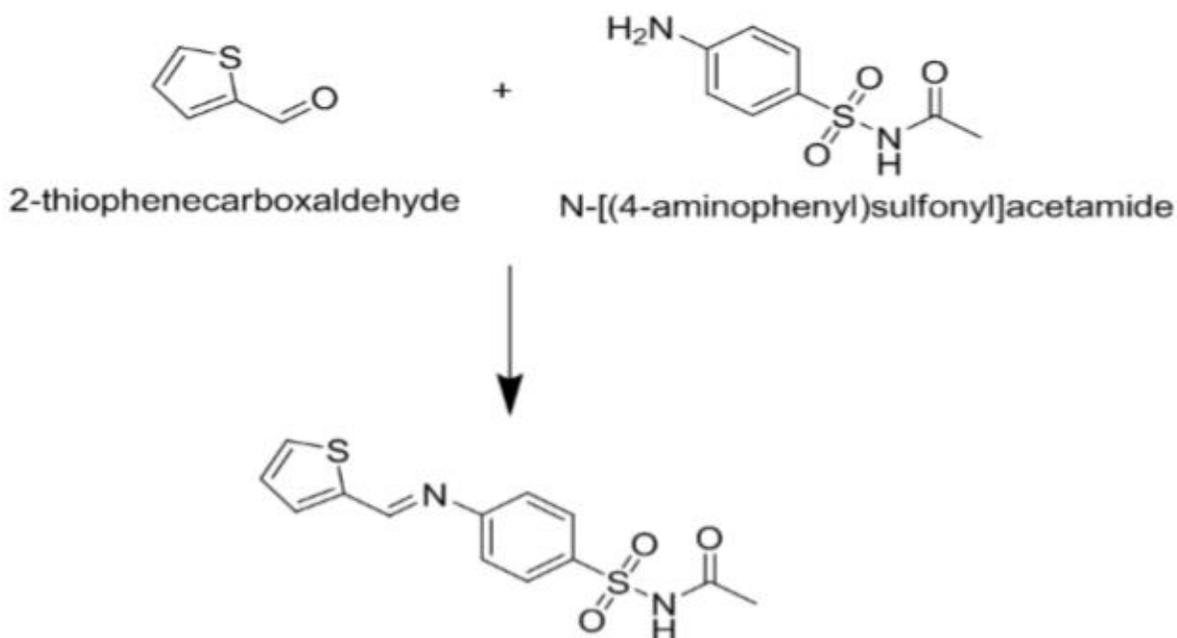


Figure17: Condensation reaction between 2-thiophenecarboxaldehyde and sulfacetamide give (E)-N-(4-(thiophen-2-ylmethyleneamino) phenylsulfonyl)acetamide S. TH.

With their versatile structures, redox behavior and physicochemical properties, inner transition metal complexes are often useful as chemical nucleases. The interaction of these complexes with DNA has gained much attention due to their possible applications as new therapeutic agents. The manipulation of the ligands greatly facilitates the interaction between the complexes and DNA. Metal based drugs represent a novel group of antimicrobial agents with potential applications for the control of bacterial and fungal infections. This inspires synthetic chemists to search for new metal complexes for bioactive compounds. This work presents the synthesis, characterization, antibacterial, antifungal and anticancer studies of a N-[(diphenylamino)methyl]acetamide and their metal complexes of cerium(IV), thorium(IV) and dioxouranium(VI). (L. MURUGANANDAM and K. KRISHNA KUMAR et al,2013)

### **In-vitro bioactivity test for immunomodulatory and cytotoxicity assessment Separation of human peripheral blood mononuclear cells**

Human venous blood was drawn and defibrinated. It was diluted with RPMI 1640 media and layered over histopaque. After centrifugation, the whole mononuclear cell layer was transferred, thoroughly mixed with the medium and washed by centrifugation. The final suspension was made in 1 to 5 mL RPMI 1640 medium with 10% serum. Equal amounts of cell suspension and trypan blue solution were mixed, fed into a haemocytometer. Live and dead cells were counted under phase contrast objective. (L. MURUGANANDAM and K. KRISHNA KUMAR et al,2013)

### **Anticancer screening**

The results obtained for the ligand and its complexes on the growth of Raji and Jukart cells are given in Tables 5&6. In general, an increase in growth inhibition is observed as the concentration of test compound increases. Here also metal ion complexes show more activity than the ligand. The increase of activity on complexation is considerable in the case of the Th(IV) complex whereas the other complexes show moderate activity but higher than for free L. (L. MURUGANANDAM and K. KRISHNA KUMAR et al,2013)

Table4: In-vitro bioactivity test for immunomodulatory and cytotoxicity assessment(MTT method)

S.No	Sample	Dye Exclusion	MTT
1	L	Non-toxic	Immunopotentiator at 100 ng
2	CeSO <sub>4</sub> .L	Non-toxic	Cytotoxic at 400 ng
3	Th (NO <sub>3</sub> ) <sub>4</sub> .L	Non-toxic	Immunopotentiator 100 ng
4	UO <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> .L	Non-toxic	Immunopotentiator

*(L- DPAMAce)*

Table5: Anticancer activities against Raji and Jukart Cell Lines(MTT Method)

S.No	Sample	Cell Lines	
		Raji	Jukart
1	L	Non toxic	Non toxic
2	Ce(SO <sub>4</sub> ) <sub>2</sub> .L	Down regulation at 50 ng	Non toxic
3	Th(NO <sub>3</sub> ) <sub>4</sub> .L	Up regulation at 50 ng	Up regulation at 50 ng
4	UO <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> .L	Up regulation at 50 ng	Up regulation at 25 ng

*(L- DPAMAce)*

In the Schiff base family, hydrazones constitute an important class as they contain strong donor sites, stability and flexidentacity. Azomethine linkage in hydrazones plays a crucial role towards the biological activities such as antimicrobial, anti-convulsant, antitubercular, anticancer, antioxidant, antiglycation, antidepressant, anthelmintic and analgesic activities. It is evident that, the biological activity of the hydrazone is deviated by its coordination with metal ions via azomethine Nitrogen and other donor atoms. Isoniazide is potent antitubercular agent, 4acetamidophenol (paracetamol) is an analgesic and antipyretic drug and derivatives of 4-acetamidophenol possess promising antibacterial, antifungal and antitubercular activity. One of its derivatives, 3-acetyl-4-hydroxyphenyl acetamide is found to be functional starting material for the synthesis of a wide variety of hydrazone ligands. However, no work has been reported on the synthesis of transition metal complexes of hydrazone, an asymmetrical Schiff base, derived from isonicotinoyl hydrazide and 3-acetyl-4-hydroxyphenyl acetamide. Promoted by these facts, in this paper, the synthesis and characterization of complexes of Cu (II), Co (II), Th(IV) and Zr(IV) with newly synthesized hydrazone have been carried out. The thermal analysis and

antibacterial activities of newly synthesized compounds have also been reported. (Prashant R. Mandlik and Pratik K. Deshmukh, 2020)

All the complexes derived from LH are colored and non-hygroscopic solids and are stable in air. They are insoluble in water, but soluble in coordinating solvents like DMF and DMSO. The molar conductance values of the complexes in DMF( $10^{-3}\text{M}$ ) are very low ( $3.7\text{-}11.5 \Omega^{-1} \text{cm}^2\text{mol}^{-1}$ ) indicating their non-electrolytic nature. The analytical and physical data of the ligand and its complexes are given in Table 7. The analytical data of all the complexes suggested 1:2 (metal: ligand) stoichiometry. The FAB mass spectra of the ligand and the complexes were recorded. All the spectra exhibited parent peaks due to molecular ions ( $\text{M}^+$ ). The proposed molecular formulae of these complexes were confirmed by comparing their molecular formula weights with the  $m/z$  values. The molecular ion peaks obtained were as follows:  $m/z$  312 (ligand), 717 (Co (II) complex), 770 (Cu(II) complex), 982 (Th(IV) complex) and 723 (Zr(IV)complex). These data are in good agreement with the proposed molecular formula for these complexes, In addition to the molecular ion peaks, the spectra exhibited different peaks assignable to various fragments arising from the thermal cleavage of the complexes. (Prashant R. Mandlik and Pratik K. Deshmukh, 2020)

Table6: The analytical and physical data of the compounds

Compound	Color	Molar cond. ( $\Omega^{-1} \text{cm}^2\text{mol}^{-1}$ )	Yield (%)	%Found (calcd.)				Formula Weight
				C %	N %	H %	M %	
LH	Light Yellow	-	72	61.48 (61.53)	17.96 (17.94)	5.21 (5.16)	-	312
$[\text{CoL}_2(\text{H}_2\text{O})_2]$	Dark Brown	11.50	63	53.51 (53.56)	15.60 (15.62)	4.75 (4.78)	8.18 (8.21)	718
$[\text{CuL}_2(\text{H}_2\text{O})_2].3\text{H}_2\text{O}$	Green	3.71	65	49.50 (49.51)	14.43 (14.44)	5.16 (5.19)	8.16 (8.19)	777
$[\text{ThL}_2(\text{NO}_3)_2]$	Off White	7.20	54	39.29 (39.27)	14.30 (14.31)	3.05 (3.09)	23.68 (23.71)	978
$[\text{Zr}(\text{OH})_2\text{L}_2]$	Cream	4.80	52	51.31 (51.39)	14.87 (14.98)	4.35 (4.31)	12.15 (12.20)	747

<sup>1</sup>H NMR spectrum of ligand

The Schiff base, (E)-N-(4-hydroxy-3-(1-(2-isonicotinoylhydrazono)ethyl)phenyl) Acetamide coordinates to the Co(II), Cu(II), Th(IV) and Zr(IV) metal ions (1:2 mole ratio) as a monobasic bidentate ligand using the azomethine Nitrogen and phenolic Oxygen donor atoms. Based on the analytical, conductance, thermal, spectral and magnetic moment's data, the assignment of octahedral geometry has been corroborated for Co (II) and Cu (II) complexes. The calculated spin Hamiltonian parameters from the ESR spectra of complex confirmed the distorted octahedral geometry for the mononuclear Cu (II) complex. Absence of lattice and coordinated water molecules was confirmed from the thermograms of both Th(IV) and Zr(IV) complexes. The activation energy calculated by the Freemann-Caroll and Sharp-Wentworth methods are in good agreement with each other. Based on chelation theory, the enhanced biological activity of the complexes over the ligand was observed. The probable structures of complexes are shown below, Figure18. . (Prashant R. Mandlik and Pratik K. Deshmukh, 2020)

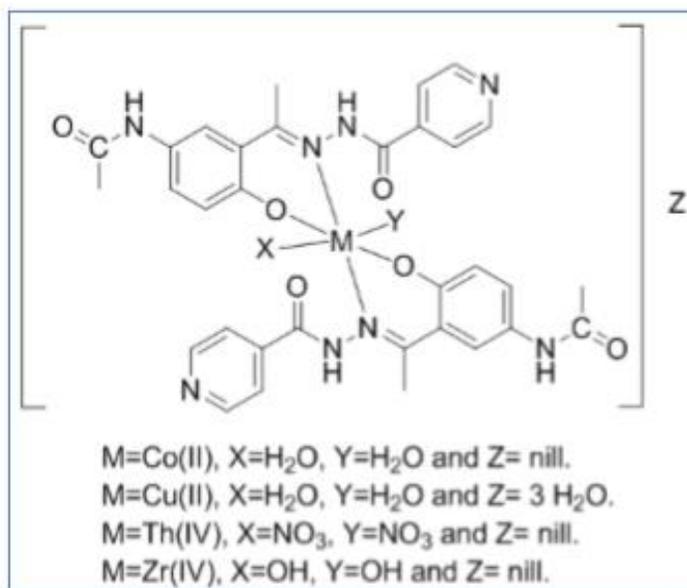


Fig18: The probable structure for Co (II), Cu(II), Th(IV) and Zr(IV) metal complexes.

Of all fields of chemistry, the study of the nucleic acids is perhaps the most exciting, taking into account that these compounds control heredity on the molecular level. The backbone of the nucleic ribonucleic acid molecule is a polyester chain (called a polynucleotide chain) derived from phosphoric acid and a sugar. Adenine is a purine nucleic base displaying a noticeable variety of monodentate and bidentate bridging

metal coordination modes and, as a consequence has been extensively studied. Complexes of thallium (I) ion with adenine and adenosine at different temperatures and constant ionic strength. Also synthesis and characterization of mixed Ligand complexes of caffeine, adenine and thiocyanate with some transition metal ions Co(II), Ni(II), Cu(II), Zn(II) and Cd(II). Mixed ligand complexes of copper (II) with dimethylglyoxime as primary ligand and purines bases (adenine, guanine) and orthophenylenediamine as a secondary ligands were prepared and characterized by elemental analysis, conductivity measurements, IR and UV-visible spectroscopy and cyclic voltametric. (Hiba A. Ghani and Basima M. Sarhan, 2020)

### Molar Conductivity (AMP)

The values of molar conductivity of the ligand (AMP) with some their metal complexes in DMSO solvent, indicated the non-electrolyte behavior of these complexes. And some of properties are shown in Table7. (Hiba A. Ghani and Basima M. Sarhan, 2020)

Table7: Some of properties of the ligand(AMP) and their metal complexes.

Compound	M.w g.mol <sup>-1</sup>	Color	M.P <sup>o</sup> C	Molar Cond. Ohm <sup>-1</sup> cm <sup>2</sup> mol <sup>-1</sup>	Yield (%)	Elemental analysis(%)calc.(found)				
						C	H	N	S	M
AMPC <sub>4</sub> H <sub>8</sub> N <sub>6</sub> OS	236	Yellow	120-122	1.03	71	40.68 (40.67)	3.39 (3.12)	35.59 (35.24)	13.55 (13.22)	–
[Mn(AMP) <sub>2</sub> Cl <sub>2</sub> ]	597.94	Deep yellow	300 d	3.99	66	32.11	2.67	28.09	10.70	9.21 (8.90)
[Co(AMP) <sub>2</sub> Cl <sub>2</sub> ]	601.93	DarkPurple	310 d	3.22	68	31.89 (31.11)	2.65 (2.48)	27.91 (27.43)	10.63 (10.65)	9.82 (9.41)
[Ni(AMP) <sub>2</sub> Cl <sub>2</sub> ]	601.71	Green	280-282	4.09	73	31.90	2.65	27.92	10.63	9.78 (9.34)
[Cu(AMP) <sub>2</sub> Cl <sub>2</sub> ]	606.54	Deep Brown	290-291	3.72	75	31.65 (31.93)	2.63 (2.05)	27.69 (27.85)	10.55 (10.9)	10.51 (10.12)
[Zn(AMP) <sub>2</sub> Cl <sub>2</sub> ]	608.38	Deep yellow	250-200	11.67	62	31.55	2.62	27.61	10.51	10.70 (10.52)
[Cd(AMP) <sub>2</sub> Cl <sub>2</sub> ]	655.4	Deep yellow	225-227	11.9	77	29.63 (29.95)	2.44 (2.83)	25.63 (25.89)	9.76 (9.85)	17.2 (16.88)
[Hg(AMP) <sub>2</sub> Cl <sub>2</sub> ]	743.6	Deep yellow	320 d	12.12	74	25.82	2.15	22.59	8.60	26.97

d = decompose

The coordination chemistry of amide group is one of the most active researchfields in organic chemistry due to its diverse coordinating behaviour and their role it plays in biological process. Carl Mannich was the first to recognize the enormous

significance of this reaction types and this reaction how arrives his name has developed into one of the most important C-C bond forming reactions in organic Chemistry. Mannich reaction is an organic reaction and it is method for the preparation of  $\beta$ -amino ketones and aldehydes and is an example of nucleophilic addition of an amine to a carbonyl group followed by dehydration to the Schiff base. The Schiff base is an electrophile which reacts in the second step with a compound containing an acidic proton as included in equation below. Mannich reaction is considered a condensation reaction and is a threecomponent condensation in which a compound containing an active H atom is allowed to react with aldehyde or ketone and a secondary amine. (Amaaly Al-Assafe and Bara S. Dobony, 2019)

## **a-Materials and Methods**

The transition metal ions were used as supplied by Fluka. All reagents used analytical grade. Molar conductance were carried out for  $10^{-3}$ M solution in dimethyl sulfoxide (DMSO) using an electronic conductivity measuring device model LF\_42 at  $25^{\circ}\text{C}$ . IR spectra were recorded by using KBr pellets. The electronic spectra of complex were recorded on Shimadzu uv.1800 spectrophotometer at  $25^{\circ}\text{C}$  using 1 cm quartz cell. Magnetic susceptibility measurements were performed on MSB\_MKI (magnetic susceptibility balance) Sherwood scientific using Gouy method Metal analysis was carried out by using an AA 240FSVarian instrument for atomic absorption Carbon, hydrogen and nitrogen contents were determined at the Ibn Haithem Centre for research, Baghdad, Iraq. (Amaaly Al-Assafe and Bara S. Dobony, 2019)

## **b-Preparation of N-(1-Morpholino (3-methoxy, 4hydroxy) benzyl]acetamide (MBA)**

For the preparation of MBA ligand employing the Mannich synthetic route. Acetamide(0.1mol,2.9g) and vaniline (3-methoxy, 4-hydroxy benzaldehyde)(0.1mol,7.69g), morpholine (0.1mol,4.3 ml) were taken in (1:1:1) mole ratio ice cold condition Acetamide was dissolved in minimum quantity of ethanol and mixed with morpholine.and stirred in ice-bath at  $5^{\circ}\text{C}$  and stirred to get a clear solution. Vaniline was dissolved in ethanol and then added in dropwise with strring in ice-bath for an hour. The resulting reaction mixture was kept at room

temperature for Ca.5d. The solid product form was filtered washed with water and ethanol removes the unreacted acetamide and morpholine. The product, MBA was then dried and recrystallized in an ethanol purity of the compound was checked by TLC. The preparation of the ligand may be represented as figure19. (Amaaly Al-Assafe and Bara S. Dobony, 2019)

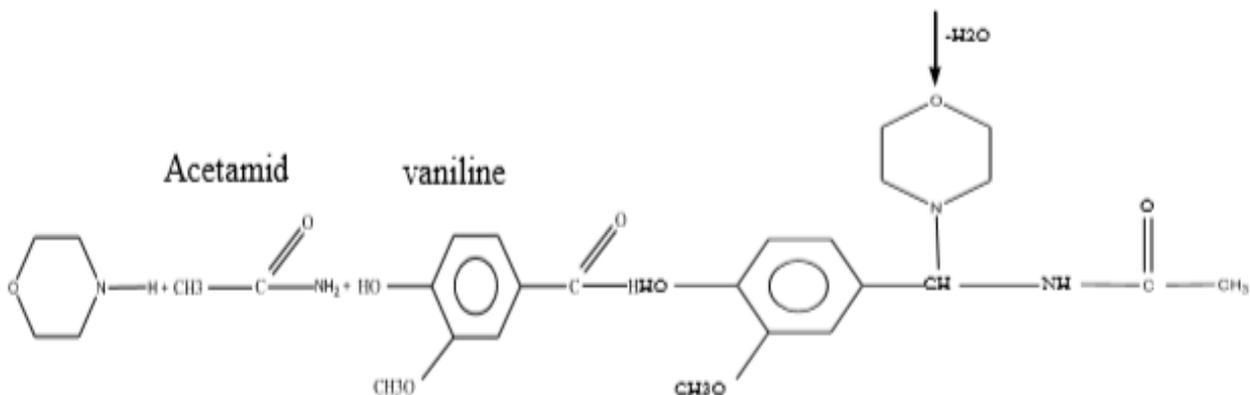


Figure19: preparation of ligand (MBA).

The acetamide and their derivatives have diverse applications in coordination chemistry, photophysics, photochemistry and bioinorganic chemistry. Three component condensation reaction of acetamide is very important for the synthesis of various useful compounds. Over the past few decades, Mannich base reactions of acetamide have been the guiding tent for the synthetic chemists because of their widespread pharmaceutical importance i.e. antibacterial, anthelmintic, antifungal, anti-inflammatory, antiviral and analgesic properties. In addition to their biological importance, acetamide form stable complexes with various transition metals. Transition metal complexes of 2-furyl methyl ketone, benzaldehyde and acetamide-based mixed ligands have been reported with bi-dentate coordination behavior. Continuous increase in bacterial resistance to existing drugs has been resulted due to wide spread use of antibacterial agents leading research on new substances possessing antimicrobial activity. The worthwhile biological activities of Mannich bases have been guiding for the synthesis of novel Mannich bases. The main objective of present communication is to provide a comprehensive account of N-Mannich type bases of acetamide, their chelating behavior and to highlight their potential in evolving better antimicrobial drugs. The synthesized compounds were further evaluated for their antimicrobial properties against various pathogens using MIC method. (U. Rizwan Sulthana and M. Shanmuga priya et al, 2018)

## Molar conductance

The complexes prepared are various colored, powder like, air stable, soluble in dimethylformamide (DMF) and dimethylsulfoxide (DMSO). The analytical data and some physical properties of the metal complexes were listed in table 8 and synthetic scheme of complex. The molar conductivities values showed that all the complexes are non-electrolytes nature with  $\Lambda_m = 30-45 \Omega^{-1}\text{cm}^2\text{mol}^{-1}$  in  $10^{-3}$  in DMSO solutions at room temperature. (U. Rizwan Sulthana and M. Shanmuga priya et al, 2018)

Table 8: Physical characterization, Analytical, Molar conductance Magnetic susceptibility data

Compound	Colour	Found/Calculated					Yield %	$\Lambda_m$ Mho $\text{cm}^2 \text{mol}^{-1}$	$\mu\text{-eff}$ B.M
		M%	C%	H%	N%	Cl%			
FBA $\text{C}_{15}\text{H}_{15}\text{NO}_3$	Colourless	-	70.02 (70.03)	5.88 (5.83)	5.44 (5.45)	-	78	-	-
Mn(II) Complex	pink	11.27 (11.29)	36.88 (36.90)	3.89 (3.90)	2.86 (2.88)	28.68 (28.69)	64	12.25	5.72
Co(II) Complex	pink	12.93 (12.94)	39.47 (39.49)	3.28 (3.29)	3.07 (3.08)	30.70 (30.72)	68	6.07	4.38
Ni(II) Complex	green	12.74 (12.76)	39.56 (39.58)	3.29 (3.31)	10.54 (10.56)	30.76 (30.77)	68	10.27	3.52
Zn(II) Complex	Colourless	13.15 (13.16)	36.43 (36.45)	3.03 (3.06)	2.83 (2.86)	28.34 (28.35)	61	6.92	--

Metal complexes of Schiff bases have been studied extensively because of their interesting structural and spectral properties of Schiff bases derived from heterocyclic amines and their metal complexes exhibit a wide variety of biological activities. Literature survey reveals that no reports are available on transition metal complexes of Schiff bases derived from 2-4 Diamino-5-chloro thiazole. In present communication we report synthesis characterization and microbial activities of CoII, NiII, CuII and ZnII complexes of Schiff base derived from 2-4 Diamino-5-chloro thiazole and hydroxyaldehyde. (R = H, 5-CH<sub>3</sub>). (BN Muthal and BN Raut, 2015)

The complexes are crystalline solid do not show sharp melting points and are soluble in common organic solvents. The elemental analysis data suggest that the complexes possess 1:1 stoichiometry. The molecular weight determination data shows that the complexes are monomeric and dimeric in nature. The very low conductance values of complexes in nitrobenzene solution indicates that the complexes are non-electrical in nature. Elemental analysis data given in table-10. (BN Muthal and BN Raut, 2015)

## Electronic Spectra

The electronic spectra of Co<sup>II</sup> complex exhibits prominent two transition band at ~6600 ( $\nu_2$ ), ~1500 ( $\nu_3$ )  $0\text{m}^{-1}$  corresponding to transition  $4T_1(P) \leftarrow 4A_2(\nu_2)$ ,  $4T_1(F) \leftarrow 4A_2(\nu_3)$  respectively. Occurrence of these transition bands suggests a tetrahedral geometry for complexes. Magnetic moment values of complexes (4.5, 4.6 BM) support the tetrahedral geometry proposed for the complexes. The electronic spectra of Ni<sup>II</sup> complexes exhibits three bands at ~9000, ~13400 and ~22000  $\text{cm}^{-1}$ . Three bands attributed to  $\nu_1$ ,  $\nu_2$  and  $\nu_3$ .  $1B_1 \leftarrow 1A_{1g}(\nu_1)$ ,  $1A_{2g} \leftarrow 1A_{1g}(\nu_2)$  and  $1E_g \leftarrow 1A_{1g}(\nu_3)$  There bands are observed in the reflectance mode and its solution spectra shows band at 14000 and 16000  $\text{cm}^{-1}$ . Occurrence of these transition band suggests square-planar geometry. The Ni<sup>II</sup> complexes are diamagnetic in character. Electronic spectra of Cu<sup>II</sup> complexes exhibits a board band at ~7400  $\text{cm}^{-1}$  suggesting a square-planar geometry. The magnetic moment values of complexes (1.9, 2.0 BM) supports the square-planar geometry proposed for the complexes. Electronic spectra of Zn<sup>II</sup> complexes exhibits a electronic absorption band at ~17000  $\text{cm}^{-1}$ , hence be assigned four coordinated square-planar structure the complexes are diamagnetic. (BN Muthal and BN Raut, 2015)

Table9: Elemental analytical data of Schiff base and the metal complexes.

Sr. No.	Formula of complex	Nature	Colour	Elemental analysis					Molecular weight	Neff (B.M.)
				C% Found (Cal)	H% Found (Cal)	N% Found (Cal)	S% Found (Cal)	Cl% Found (Cal)		
1	[Co(Sal) <sub>2</sub> DCT]	Crystalline	Blue	49.22 (49.28)	2.35 (2.41)	10.05 (10.14)	7.70 (7.79)	8.35 (8.45)	407 (413.94)	4.5
2.	[Ni(Sal) <sub>2</sub> DCT]	Crystalline	Ochre Yellow	49.20 (49.31)	2.30 (2.41)	10.05 (10.15)	7.69 (7.73)	8.41 (8.46)	408 (413.69)	Diamagnetic
3.	[Cu(Sal) <sub>2</sub> DCT]	Crystalline	Dirty gray	48.55 (48.73)	2.34 (2.38)	9.95 (10.03)	7.59 (7.64)	8.22 (8.36)	410 (418.57)	1.9
4.	[Zn(Sal) <sub>2</sub> DCT]	Crystalline	Cream Yellow	48.44 (48.52)	2.33 (2.37)	9.81 (9.99)	7.57 (7.61)	8.25 (8.32)	409 (420.38)	Diamagnetic
5.	[Co(5ms) <sub>2</sub> DCT]	Crystalline	Blue	51.48 (51.59)	3.06 (3.16)	9.45 (9.50)	7.17 (7.24)	7.88 (7.91)	438 (441.94)	4.6
6.	[Ni(5MS) <sub>2</sub> DCT]	Crystalline	Ochre Yellow	51.49 (51.61)	3.07 (3.16)	9.41 (9.50)	7.18 (7.24)	7.89 (7.42)	437 (441.69)	Diamagnetic
7.	[Cu(Sal) <sub>2</sub> DCT]	Crystalline	Dirty gray	50.90 (51.05)	3.03 (3.13)	9.34 (9.40)	7.08 (7.16)	7.77 (7.83)	442 (446.57)	2.0
8.	[Zn(Sal) <sub>2</sub> DCT]	Crystalline	Cream Yellow	50.77 (50.84)	3.08 (3.12)	9.31 (9.36)	7.04 (7.13)	7.74 (7.80)	443 (448.38)	Diamagnetic

The history of metal- paracetamol complexes began when researchers arrived at the possibility of paracetamol chelating with some heavy metals, as Acetaminophen usually coordinate as a bidentate ligand through a hydroxyl group located on the benzene ring, forming H-O-M and a carbonyl group, producing C=OM. The coordination manner of C=O-M was reported for some transition metals and confirmed mostly by infrared red techniques. A good illustration of this is the formation of Copper-paracetamol complexes that were made at borate buffer in the presence of sodium nitrate. The authors used Mass spectrometry and Nuclear Magnetic Radiation (NMR) to propose the product's structure and indicated the copper. is coordinated to the chelating ligand via the amine and carbonyl groups. The system was found to have a stoichiometric ratio of 1:1 for the metal and ligand. Lawal, A., and Obaleye reported the synthesis of Co(II), Ni(II), Fe(III) with aspirin and paracetamol. These coordination compounds exhibited 1:1 ratio metal to ligand, where the Complexation was observed via OH, and C=O group. Furthermore, Aderoju a. Osowole et. studied paracetamol complexes with Copper (II) chloride tetrahydrate, Nickel(II) chloride hexahydrate, Cobalt (II) chloride hexahydrate, Manganese (II) chloride tetrahydrate, Zinc (II) nitrate hexahydrate, and Zinc (II) acetate dehydrate and percentage metal, magnetic and spectroscopic data were employed to suggest a reasonable structure.<sup>16</sup> It was observed that these materials gave a proposed structure with 1:2 ratio metal to ligand, where the ligand was bounded to the metals through hydroxyl and carbonyl groups. (Mohanad A. Sultan and Ali E. Karim et al, 2020)

In addition, Acetaminophen acts as a bidentate ligand via amine and carbonyl groups. Research area on this coordination form was not extensively investigated; only few metals complexes were reported. Mg (II), Ca (II), Ba (II), Sr (II) display complexes with paracetamol in which the metal connected to the ligand through the lone pair of nitrogen and the carbonyl amide unit and these phases found to have 1:2 stoichiometric ratio for the metals and the ligand. (Mohanad A. Sultan and Ali E. Karim et al, 2020)

The complex was confirmed to be stable. It was a nonhygroscopic material with a higher melting point, indicating the complex is more stable than the free ligand. The complex was black in color. To confirm the chemical structure of the complex, both IR and UV-visible light instruments were employed. The structure determination of the complex was carried out based on the comparison of the spectrum of free paracetamol with the spectrum of its metal complex. (Mohanad A. Sultan and Ali E. Karim et al, 2020)

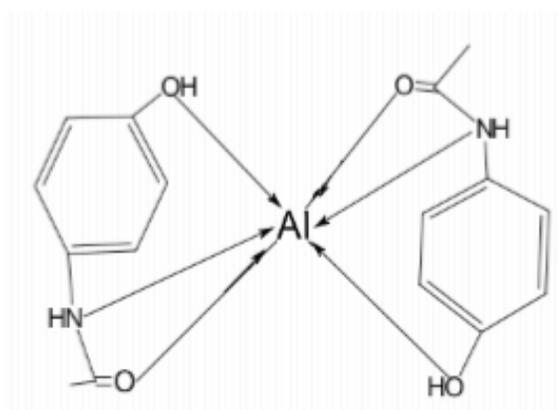


Figure20: A proposed structure of Al(III) complex

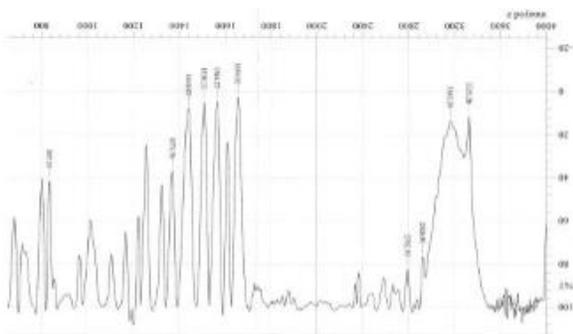


Figure21: FTIR spectrum of free Paracetamol

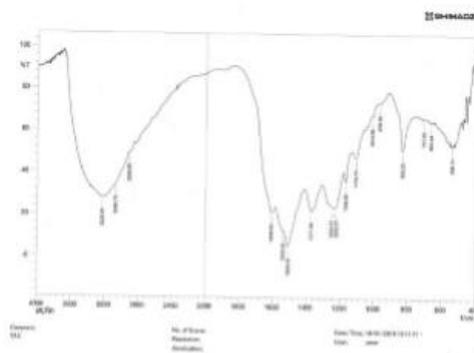


figure22: FTIR spectrum of Al(III)-Paracetamol complex

There has been a significant exploitation in recent years towards the formulation of new materials containing polyfunctional units (ligands) able to coordinate with metallic ions. Schiff base macroligands are synthesized from the reaction of aldehydes and amino compounds. In recent years, the chemistry of transition metal complexes, mainly of those derived from N-donor ligands, remained focalized by several researchers, due to their significant applications in organic synthesis, new materials, catalysis and medicinal science (e.g. antitumor drugs). The synthesis of metal complexes of these ligands also gaining importance in growing area of research of applied inorganic chemistry. Metal complexes of Schiff bases are extensively studied due to synthetic flexibility, selectivity and sensitivity towards a variety of metal atoms. They are found useful in catalysis, in medicine as antibiotics, anti-inflammatory agents and in the industry as anticorrosion. (TARIQ MAHMUD and RABIA REHMAN et al, 2012)

The Schiff base (N-[4-(Phenyliminomethyl)phenyl]acetamide) 0.67-hydrate, was prepared and characterized in our previous research work. In the following study, its metal complexes were synthesized and analyzed. Figer31 is showing the proposed scheme of the chemical reaction involving in synthesis of Schiff base (N[4(Phenyliminomethyl)phenyl]acetamide). (TARIQ MAHMUD and RABIA REHMAN et al, 2012)

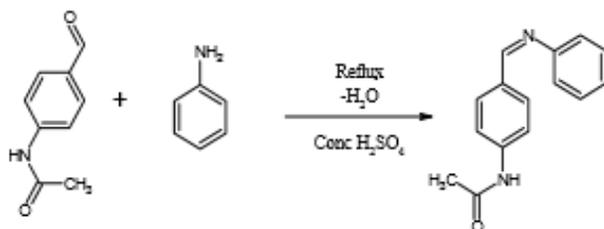


Figure23: Synthesis of Schiff base (N-[4-(Phenyliminomethyl)phenyl]acetamide) 0.67 Hydrate

Mannich base complexes have remained an important and popular area of research due to their simple synthesis, adaptability, and diverse range of applications. From the survey of existing literature, it appears that metal complexes of Mannich bases played a vital role in the development of coordination chemistry. Many potent antibacterial and antifungal compounds synthesized by the condensation of aldehyde, amine and amide have been reported. Organic chelating ligands containing amide moiety as a functional group have a strong ability to form metal complexes and exhibit a wide range of biological activities. Literature studies revealed that during the past decades, there has been a great deal of interest in the synthesis and structural elucidation of transition metal complexes containing amide moiety. However, there is no study on any metal complexes of N-[(Diphenylamino) methyl]acetamide (DPAMAce). In the present work, Mannich base derived from the condensation of benzaldehyde, diphenylamine and acetamide, and its metal complexes with Zn(II), Cd(II) and Hg(II), are synthesized and are characterized using different physicochemical techniques. The ligand and its metal complexes have biological activity against various microbes were tested in vitro against six bacterial species and two fungal species by disc diffusion method. (L. MURUGANANDAM and S. Selvam et al,2015)

## Antimicrobial studies

Antimicrobial activities of DPAMAc and their two metal complexes were tested in vitro against six bacterial species *E.coli*, *P.aeruginosa*, *S.typhi*, *B.subtilis*, *S.pyogenes* and *S.aureus* and the fungal species *A. niger* and *A.flavus* by disc diffusion method using agar nutrient as medium and gentamycin as control. The paper disc containing the compound (10, 20 and 30  $\mu\text{g}/\text{disc}$ ) was placed on the surface of the nutrient agar plate previously spread with 0.1 mL of sterilized culture of microorganism. After incubating this at 37°C for 24 hrs, the diameter of inhibition zone around the paper disc was measured. (L. MURUGANANDAM and S. Selvam et al,2015)

The therapeutic and diagnostic properties of transition metal complexes have attracted considerable attention leading to their application in many areas of modern medicine. Many coordination compounds of transition metal ions accomplish nucleolytic cleavage. In this regard, mixed-ligand metal complexes were found to be particularly useful because of their potential to bind DNA via a multitude of interactions and to cleave the duplex by virtue of their intrinsic chemical, electrochemical, and photochemical reactivities. A singular advantage in the use of these metallo—intercalators for such studies is that the ligands or the metal ion in them can be varied in an easily controlled manner to facilitate individual applications. although DNA interactions of number of mixed-ligand complexes previously appeared in the literature, there is still scope to design as study Schiff base with metal salt as new chemical nucleases. Bearing these facts in mind, the nuclease activity of mixed ligand complexes of Cu(II) and Zn(II) containing Schiff base is reported in here. DNA binding was also searched. Hence, the present study is very valuable in understanding the mode of complex binding to DNA, as well as laying the foundation for the rational design of DNA structure and antitumor drugs. (Omar H. Al-Obaidi,2012)

## Electronic Absorption Spectra

The UV-Vis Spectra of the complexes were recorded in DMSO solution. In addition, the complexes exhibited intense bands in the 215 - 265 nm region, which are attributed to charge transfer transitions. The intense higher energy bands at around 215 nm can be attributed to intraligand  $\pi-\pi^*$  transitions. The copper complexes showed

magnetic moment values in the range of 1.85 - 1.88  $\mu_B$  which indicate the monomeric nature of the complexes and characteristics for a distorted octahedral structure. The zinc (II) complexes showed bands at 215 and 260 nm, assigned to intra-ligand charge transfer transitions. They are diamagnetic. Based on the magnetic moment, electronic and IR data, the proposed structures of the complexes are given in Figure24. (Omar H. Al-Obaidi,2012)

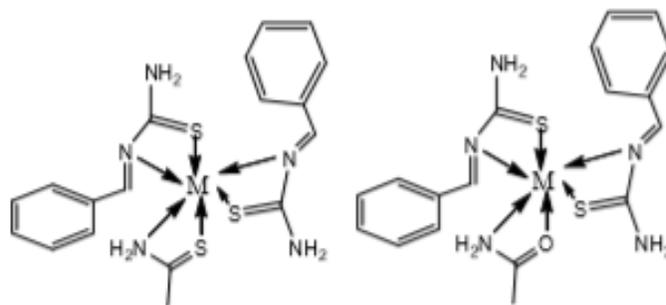


Figure24: The structural formulas of the complexes  $[M(L1)_2(L2)]Cl_2$  and  $[M(L1)_2(L3)]Cl_2$ ,  $M=Cu(II)$  or  $Zn(II)$

Synthesis and investigation of metal complexes with active pharmaceuticals, in which the drug molecules play a role of ligand, have been regarded as a research domain of increasing interest for inorganic, pharmaceutical, and medicinal chemistry. Literature survey indicated that over the last decade, there had been tremendous attention towards studies on metal complexes formation using drugs as ligand. A characteristic of metal ions is that they easily lose electrons from the familiar elemental or metallic state to form positively charged ions. Metal-containing compounds offer many advantages over conventional carbon-based compounds in the development of new medicinal compounds. These metal complexes are found to be interesting due to their biological applications like antifungal, antibacterial and anti-tumor activity. These complexes offer a great diversity in their action; they do not only have anticancer properties but have also been used as antibacterial, anti-inflammatory and anti-diabetic compounds. Acetaminophen (Figure25) otherwise known as paracetamol, is a derivative of 4aminophenol having the chemical name N-(4-hydroxyphenyl) acetamide, molecular weight 151.16 and formula  $C_8H_9NO_2$ . It is a widely used painkiller for mild to moderate pain, e.g. for headaches and muscular pains. It is useful in tooth ache and rheumatism. It also reduces fever and is available in 500 mg tablets or in liquid form for children. It is well tolerated with very few side-effects. (J. Oaley ana A.A. Aliyu et al,2021)

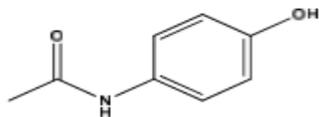


Figure25: Chemical structures of acetaminophen

Nitrogen containing biologically active compounds are of high interests as pharmaceutical products. The Mannich reaction is one of the most basic and useful methods for the synthesis of such compounds and has been widely used to introduce aminomethyl group into a variety of organic compounds. Mannich base derivatives with bridge N-atom have been found to possess a broad range of biological activities including antimicrobial, antitumor, anti-inflammatory, antipyretic and antimalarial and some of them were used as complexing agents. At the present time, metal based drugs are an important source of novel molecules with therapeutic activity. Furthermore, coordination compounds with transition metals have been investigated in the last few decades after the discovery of cisplatin because they have shown good antineoplastic activity and less toxicity. Literature survey shows that a large number of transition metal complexes of amides have been found to be associated with diverse pharmacological activities. Complexes of transition metals with amides in proteins and peptides are utilized in numerous biological processes, such as oxygen conveyer, electron transfer and oxidation. In these processes, the enzymatic active site, which is very specific, forms complexes with divalent metal ions. (L. MURUGANANDAM and S. Selvam et al,2017)

IR spectrum of PBA shows a sharp band at  $3306\text{ cm}^{-1}$  is assigned to  $\nu_{\text{NH}}$  stretching vibration of the secondary amide group. The medium bands at  $3053$  &  $3035$ ,  $2821$  and  $2971$ & $2876\text{ cm}^{-1}$  are attributed to aromatic, aliphatic and alicyclic (C-H) stretching vibrations respectively. The strong band at  $1646\text{ cm}^{-1}$  may be attributed to the  $\nu_{\text{C=O}}$  stretching mode. The medium absorption band appears at  $1149\text{ cm}^{-1}$  may be assigned to the new C-N-C bond formed due to the formation of Mannich base by the insertion of pyrrolidinobenzyl group on acetamide. The absorption band at  $1126$  &  $1077\text{ cm}^{-1}$  assigned to the C-N-C frequency of pyrrolidine. (L. MURUGANANDAM and S. Selvam et al,2017)

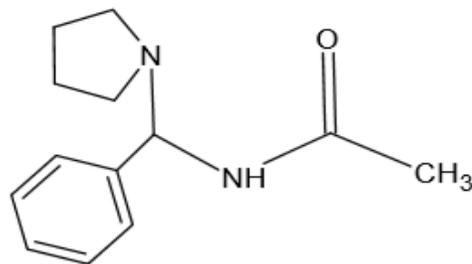


Figure26: N-[Phenyl(pyrrolidin-1-yl)methyl]acetamide(PBA)

There had been increasing studies of Mannich base complexes over the years due to the selectivity and sensitivity of the ligands to various metal ions. The quest of a coordination chemist is directed at designing ligands and acquiring more understanding of the ways in which they complex with metal ions. Metal ion complexes act as catalysts and it is necessary to design more effective catalysts for a variety of metal catalyzed ligand reactions. Mannich bases are  $\beta$ -amino carbonyl compounds produced from the condensation of ammonia or primary/secondary amine, with formaldehyde and a compound containing at least one hydrogen atom of pronounced reactivity to give an amide functional group. Mannich reaction find applications in the synthesis of many natural products and biologically important compounds and it is one of the most fundamental and important C-C bond forming reactions in organic synthesis. Organic chelating ligands containing amide moiety as a functional group have a strong ability to form metal complexes and exhibit a wide range of biological activities, Mannich bases have played a vital role in the development of coordination chemistry. Mannich bases exhibit complexation characteristics with many transition metal ions. These complexes remain an important and growing area of research due to their simple synthesis, adaptability and diverse range of applications. Many potent antibacterial and antifungal compounds synthesized by the condensation of aldehyde, amine and amide have been reported. (Nduaguba, C.B. and Durosinmi, L.M. et al,2018)

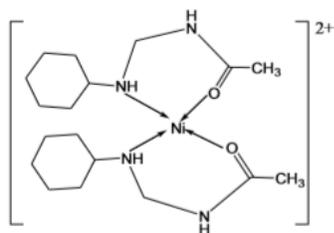


Figure27: Nickel(II)-CHMAA

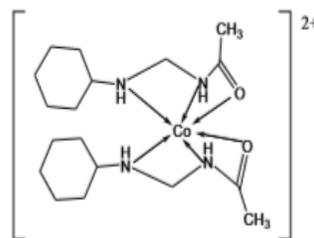


Figure28: Cobalt(II)-CHMAA

## References:

- Abu-Khadra, A.S., Afify, A.S., Mohamed, A., Farag, R.S. and Aboul-Enein, H.Y., 2018. Preparation, Characterization and Antimicrobial Activity of Schiff Base of (E)-N-(4-(Thiophen-2-ylmethyleneamino) Phenylsulfonyl) Acetamide Metal Complexes. *The Open Bioactive Compounds Journal*, 6, pp. 1-10.
- Al-Assafe, A. and Al Dobony, B.S., Synthesis and Characterization of some New Complexes of Fe (II), Co (II), Ni (II) and Cu (II) Ions with Mixed Ligands Derived from Mannich Bases and Diamine Ligands. *International Journal of Recent Research and Review*, 12(1).
- Al-Merhj, S.A., 2012. Synthesis and characterization of new thiourea complexes. *journal of the college of basic education*, 18(73).
- Al-Obaidi, O.H., 2012. Synthesis, Characterization and Antimicrobial Screening Mixed-Ligand Cu (II) and Zn (II) Complexes; DNA Binding Studies on Cu (II) Complex. *Open Journal of Inorganic Non-metallic Material*, 6, pp. 59-64.
- AYENI, A.O., WATKINS, G.M. and HOSTEN, E.C., Impact of Thiocyanate on Catalytic Abilities of Metal Complexes of 4-N-(4-hydroxy-3-((piperidin-1-yl) methyl) phenyl) acetamide (HL). X-ray Crystal Structure of HL. *Rivista de Chimie*, 71(9), pp. 143-152.
- Ghani, H.A. and Sarhan, B.M., SYNTHESIS AND SPECTROSCOPIC STUDY OF N-(METHYLCARBAMOTHIOYL) ACETAMIDE WITH THEIR METAL COMPLEXES. *Biochemical and Cellular Archives*, 20(1), pp. 2309-2316.
- Mahmud, T., Rehman, R. and Anwar, J., 2012. Synthesis, Analytical and Antibacterial Studies of N-[4-(phenyliminomethyl) phenyl] acetamide 0.67-hydrate and its... *Journal Chemical Society of Pakistan*, 34(1), p.67.
- Mandlik, P.R. and Deshmukh, P.K., 2020. Synthesis, Spectroscopic Characterization, Thermal Analysis and Biological Studies of Hydrazone Schiff Base and its Co (II), Cu (II), Th (IV) and Zr (IV) Metals Complexes. *Saudi J. Med. Pharm. Sci*, 6(12), pp.724-732.
- Muruganandam L, Krishnakumar K. Synthesis, characterization and antimicrobial studies of a new mannich base n-[morpholino (phenyl) methyl] acetamide and its cobalt (ii), nickel (ii) and copper (ii) metal complexes. *E-journal of chemistry*. 2012 Apr 1;9(2):875-82.

Muruganandam, L., Kumar, K.K. and Balasubramanian, K., 2013. Synthesis, characterization, antibacterial, antifungal and anticancer studies of a new antimetabolite: N-[(Diphenylamino) methyl] acetamide and some of its inner transition metal chelates. *Chemical Science Transactions*, 2(2), pp.379-384.

Muruganandam, L., Selvam, S. and Kanimozhi, V., 2015. SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL STUDIES OF SOME d 10 METAL COMPLEXES WITH A NEW MANNICH BASE N-[(DIPHENYLAMINO) METHYL] ACETAMIDE. *Asian Journal of Pharmaceuticcal Sciences and Technology*, 5(2), pp.93-97.

Muruganandam, L., Selvam, S. and Venkatachalam, R., 2017. A NEW MANNICH BASE N-[PHENYL (PYRROLIDIN-1-YL) METHYL] ACETAMIDE- SYNTHESIS, SPECTRAL PROPERTIES, ANTIBACTERIAL AND ANTIFUNGAL STUDIES OF SOME OF ITS METAL COMPLEXES. *WORLD JOURNAL OF PHARMACEUTICAL RESERCH*, 6(7), pp. 1481-1493.

Muthal, B.N. and Raut, B.N., 2015. Synthesis and Characterization of CoII, NiII, CuII and ZnII. Schiff Base Complexes and Their Microbial Activities. *The Pharma Innovation*, 4(7), pp.01-05.

Nduaguba, C.B., Durosinmi, L.M. and Egharevba, G.O., 2018. Synthesis and characterization of cobalt (II), nickel (II) and copper (II) complexes of Cyclohexylamine-N-methyl Mannich base ligands. *Ife Journal of Science*, 20(2), pp.237-251.

Obaleye, J.A., Aliyu, A.A., Rajee, A.O. and Bello, K.E., 2021. Synthesis, characterization, in-vitro anti-inflammatory and antimicrobial screening of metal (II) mixed diclofenac and acetaminophen complexes. *Bulletin of the Chemical Society of Ethiopia*, 35(1), pp.77-86.

Padusha, M.S.A. and Krishnaveni, G., 2018. Synthesis, Spectral Characterisation and Antibacterial Activity of metal complexes derived from the mannich base, n-(3-(furan-2-yl)-3-oxo-1-phenylpropyl) acetamide. *International Journal of Creative Reasearch Thoughts*, 6(1), pp.801-807.

Sarhan, B.M., Waheed, E.J. and Kadhim, N.J., 2016. Synthesis and Characterization of Some Metal Complexes of [2-chloro-N-(1, 5-dimethyl-3-oxo-2-phenyl-2, 3-dihydro-1H-pyrazol-4-ylcarbamothioyl) acetamide](L). *Journal University of Kerbala*, 14(3)

Sultan, M.A., Karim, A.E., Kandory, A. and Al-metwali, A., Synthesis and characterization of Al (III) complex with paracetamol. *International Journal of Pharmaceutical Quality Assurance*.10(1),pp. 156-159



## ئالوزە ى ئە سىتتە مايدى توخمە گواستراوہ کان

پروژەى دەرچوونە  
پیشکەش بە بەشى (کیمیا) کراوہ ، وەك بەشیک له  
پیداویستیەکانى بە دەستپینانى پروانامەى بە کالۆریۆس له  
زانستى (کیمیا)

ئامادە کراوہ لە لایەن:-  
ساقان کامەران علی

بە سەرپەرشتى:-  
م. محمد حاجى

نيسان - 2022