SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF SCHIFF BASES AND THEIR METAL COMPLEXES

Thesis submitted to
the University of Calicut in partial fulfilment of the
requirements for the award of the degree of

Doctor of Philosophy
in Chemistry under the Faculty of Sciences
by

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Under the guidance of
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21.12.2018

Certificate

This is to certify that the thesis entitled, ***"Synthesis, Characterization and Biological evaluation of Schiff bases and their Metal complexes"*** *is an authentic record of the research work carried out by* **Mr. SUBIN KUMAR. K,** *under my supervision and guidance in partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Chemistry under the Faculty of Sciences, Department of Chemistry, University of Calicut, Kerala and further that no part thereof has been presented before for any other degree.*

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Certificate

This is to certify that the corrections/suggestions from the adjudicators have been incorporated in the thesis entitled **“Synthesis, Characterization and Biological Evaluation of Schiff bases and their Metal Complexes”** submitted by **Mr. Subin Kumar. K**, under my supervision in partial fulfillment of the requirements for the Degree of **Doctor of Philosophy in Chemistry**, under the Faculty of Sciences of the University of Calicut. The publications have been included at the end of the thesis.

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Declaration

I, **Subin Kumar K.**, hereby declare that this thesis entitled, **"Synthesis, Characterization and Biological evaluation of Schiff bases and their Metal complexes"**, submitted to the University of Calicut in partial fulfilment of the requirements for the award of Doctor of Philosophy in Chemistry, is a bonafide research work done by me under the supervision and guidance of **Prof. Dr. K. K. Aravindakshan**.

I further declare that this thesis has not previously formed the basis for the award of any other degree, diploma or other similar title.

SUBIN KUMAR. K

Calicut University
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Preface

Compounds containing an azomethine group (-CH=N-) are known as Schiff bases. They are known since 1864 when Hugo Schiff synthesized and reported the condensation product of primary amines with carbonyl compounds. Schiff bases and their metal complexes could be applied in different areas such as separation processes, bioinorganic chemistry, catalysis, electro chemistry and environmental chemistry. Schiff bases complexes continue to attract many researchers because of their wide applications in various industrial, analytical and pharmaceutical fields. Active methylene compounds are synthetically important compounds and their Schiff bases are reported to show striking antimicrobial- and anticancer activities. Therefore, it was decided to synthesize and characterize metal complexes of mixed Schiff bases ligands derived from different active methylene compounds and aromatic ketones with 1,2-ethylenediamine.

Various applications of Schiff bases and their complexes prompted us to undertake this investigation. Therefore, in the present investigation we have synthesized and characterized 6 novel Schiff bases derived by the condensation of 2 different carbonyl compounds with 1,2-ethylenediamine. The carbonyl compounds, selected were acetoacetanilide, ethyl/methyl acetoacetate, *o*-vaniline and *o*-hydroxyacetopheneone. Further, their ligational behaviors have been assessed and 52 metal complexes have been synthesized. They were characterized using different physico-chemical- and spectral techniques and geometries have been assigned to them. Aantibacterial- and antifungal activities, *in vitro* cytotoxicity and anticancer activity of selected Schiff base ligands and their transition metal complexes were studied and the results were analysed.

The thesis is divided into two parts. The Part I entitled, "Synthesis and Characterization" is further divided into 8 chapters. **Chapter I** starts with a general introduction of the history of coordination chemistry and give a very brief review of the research work carried out on coordination compounds of Schiff bases, especially those derived from acetoacetanilide, *o*-vanillin and *o*-hydroxyacetophenone with amines. **Chapter II** describes the reagents used, the methods of preparation and physico-chemical methods employed for the characterisation of the ligands and the complexes. The synthesis and characterization of complexes of VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) with the novel Schiff base ligands, acetoacetanilide-(1,2-ethylenediimine)ethylacetoacetate (AcEE), acetoacetanilide-(1,2-ethylenediimine)methylacetoacetate (AcEM), *o*-vanilin-(1,2-ethylenediimine)acetoacetanilide (VEAc), *o*-hydroxyacetophenone-(1,2-ethylenediimine)acetoacetanilide (HEAc), *o*-hydroxyacetopheneone-(1,2-ethylenediimine)ethylacetoacetate (HEE) and *o*-vanilin-(1,2-ethylenediimine) *o*-hydroxyacetophenone (VEH), are discussed in the **Chapters III, IV, V, VI, VII** and **VIII**, respectively. Thermal analyse of some of these complexes were also carried out.

In the **Part II** of the thesis is biotoxic evaluation of the compounds and is divided into two chapters. **Chapter IX** discusses the "Antimicrobial Studies". It has 2 sub-sections comprising of the determination of the antibacterial- and antifungal activities of the two ligands and their metal complexes synthesized here. This chapter starts with an introduction and has a brief review of researches carried out in the field. The experimental procedures adopted here and the results of the antibacterial- and antifungal studies undertaken are given in the sub-sections. **Chapter X** covers the "Anticancer Studies" of one of the above ligand and its metal complexes. It gives a general introduction to the methods adopted for anticancer studies, a brief review and the results and discussion.

The references cited in the text are arranged in a serial order at the end of each chapter of the thesis.

The work discussed in this thesis has been partially published as indicated below.

1. Subin kuamr. K, Priya Varma C, Reena VN, Aravindakshan. K K, Synthesis, Characterization, Cytotoxic, Anticancer and Antimicrobial Studies of Novel Schiff Base Ligand Derived From *o*-Vanillin and Its Transition Metal Complexes, ***Journal of Pharmaceutical Sciences and Research***. 9(8), 1317-1323 (**2017)**
2. Subin Kumar. K, Aravindakshan. KK, Synthesis, Characterization Antimicrobial and Antioxidant Studies of Complexes of Fe(III), Ni(Ii) and Cu(II) with Novel Schiff Base Ligand (E)-Ethyl 3-((3-Aminopropyl)Imino)Butanoate, ***Journal of Pharmaceutical Chemical & Biological Sciences***. 5(3), 177-186 (**2017)**
3. Subin Kumar. K, Aravindakshan K. K, Antitumor, Cytotoxic And Antimicrobial Studies Of A Novel Schiff Base, *ortho*-Vanillin-(1,2 Ethylenediimine)*ortho*-Hydroxyacetophenone And Its Transition Metal Complexes, ***Journal of Pharmaceutical Chemical & Biological Sciences***. 5 (3), 271-281 (**2017)**
4. Subin Kumar. K, Priya Varma. C, Reena. V. N, Aravindakshan. K. K, Cytotoxic, antitumor and antimicrobial studies of a oxygen and nitrogen donor, novel schiff base ligand, acetoacetanilide-(1, 2-ethylenediimine)ethylacetoacetate and its first series transition metal complexes, ***International Research Journal of Pharmacy***, 8(10), 160-166 (**2017)**

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To

Ramachandran & Parvathi (My parents)

PART-I

SYNTHESIS AND CHARACTERIZATION

Chapter I

INTRODUCTION

The aqua complex ions of metals must have existed on the blue planet, since the presence of dampness[1]. Subsequent evolution of life depended on, and might even have resulted from the interaction of metal ions with organic molecules. Inorganic chemistry, especially the coordination chemistry encompasses a great diversity of substances and phenomena. Coordination compounds have been a challenge to the inorganic chemists since they were identified in the nineteenth century. In the early days, they seemed unusual because they appeared to defy the usual rules of valence. Today, they comprise a large body of current inorganic research.[2] One of the important dynamic areas of research in science in the twentieth century was Alfred Werner`s development of Coordination Chemistry.[3] Werner is rightly called as father of Modern Inorganic Chemistry. Werner`s ideas were compatible with the electronic theory of valance proposed by G. N Lewis[4] which was exclusively applied to coordination compounds by Sidwick.[5]

Some metal complexes were synthesized and used in the eighteenth century itself, though their structures were not known. Most of the traditional Indian painters used mixtures of metal salts and vegetable extracts as paints for drawing on walls and fabric materials. Presumably, the metal ions reacted with the constituents of vegetable extracts and formed colored complexes. The earlier well documented metal complex was Prussian blue, $Fe[Fe(CN)_6]_3$. It was used in Germany as the artist`s paint in the beginning of the eighteenth century.[1] Then in 1798, Tassart -a French chemist, so obscure in the history of chemistry that even his first name remains unknown, observed that ammonia when reacts with cobalt ore yielded a reddish brown mahogany colored product. This was most likely the first known coordination compound. Though out the first half of the nineteenth century, many other, often beautifully crystalline examples of various cobalt ammonates were prepared.[6] This discovery encouraged other chemists to prepare many more metal complexes and thus the subject of coordination chemistry progressed. Though several coordination compounds were prepared and their properties were studied in the nineteenth century (up to 1893), very little was understood about their structure and bonding. In 1893, Werner proposed a theory on these compounds, which for the first time led to a clear understanding of the bonding in such compounds. The development of the quantum mechanical understanding of chemical bonds subsequently resulted in a clearer knowledge about the structure and bonding of the coordination compounds.

The long awaited renaissance in inorganic chemistry finally arrived during the 1940`s. Since that time there has been great activity in all branches of science, particularly in the chemistry of coordination compounds.[7] The multi prolonged research carried out in the field of coordination chemistry has played an important role in the fast development of inorganic chemistry, encompassing a great variety of subjects and phenomena. In fact, this flourishing development of inorganic chemistry in general and of coordination chemistry in particular is only about a few decades old, despite the great progress from the times of Sorphins Mads Jorgenson[8] and Alfred Werner in the field of coordination chemistry.

From 1900 - 1950, the realm of coordination chemistry continued to expand. In one of the most productive avenues of research, Alfred Werner worked through the first two decades of the new century to bring order to the mysterious set of cobalt ammonates and related compounds.[8] The tenets of Werner`s theory have not been discarded, but they have been refined and greatly extended. For example, early works considered coordination compounds of only a few metals especially platinum, cobalt and chromium and coordination numbers of four and six. Werner`s Coordination theory gave new ways to think about the structures, properties and reactions of the new class of compound, which he called ‘Coordination Compounds’[9]. Several coordination compounds, their preparations, behaviors, various physico-chemical properties and important applications in industrial, biological and medical fields have already been discussed in details in the standard texts and literatures[11-27]. The history of the development in the area of Coordination Chemistry is given in **Table. 1**

Table. 1 Historical development in Coordination Chemistry

Si. No	Name of the Scientist	Major Contribution	Year
1.	Tassart	First Cobalt ammine Complex Observed	1798
2.	Gmelin	Cobalt ammonate and oxalate synthesized	1882
3.	Genth Claudet	$CoCl_3.6H_2O$, $CoCl_3.5H_2O$ prepared	1851
4.	Blomstrand	Chain Theory of ammonates	1869
5.	Jorgensen	Expansion to Chain theory	1884
6.	Werner	Introduction to Coordination compounds	1892
7.	Werner	Postulates of Coordination theory proposed	1902
8.	Werner	Cis-trans isomer of $[CoCl(NH_3)(en)_2]X_2$ resolved	1911
9.	Werner	Non-carbon containing optical isomer resolved	1914
10.	Sidgwick	Bonding applied to Coordination compound	1927
11.	Bethe, Van Vleck	Crystal Field theory (CFT)	1933

Now, coordination chemistry is one of the important components of Inorganic Chemistry. More recent research on coordination compounds has been concerned with nearly all the metals in the periodic table, with all coordination numbers from two to twelve and in many oxidation states.[10] Milestones in the development coordination chemistry are: (**Fig. 1- 6)**

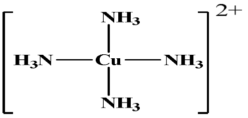
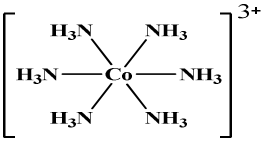
Fig. 1: Tetraminocopper(II)	**Fig. 2: Hexaminocobalt(III)**
 Tetraminocopper(II) Liban (1597)	 hexaminocobalt(III) Tassart (1796)

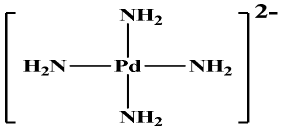
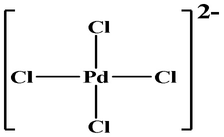
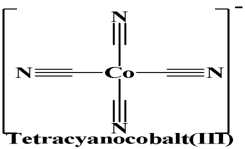
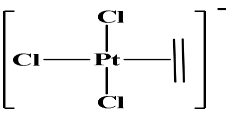
Fig. 3: Tetraminopalladium(II)	**Fig. 4: Tetrachloropalladium(II)**
 Tetraminopalladium(II) Vauqueline (1813)	 Tetrachloropalladium(II) Vauqueline (1813)

Fig. 5: Tetracyanocobalt(III)	**Fig. 6: Trichloroethyleneplatinate(II)**
 **Tetracyanocobalt(III)** **Gmeline (1822)**	 Trichloroethylene platinate(II) (Zeise`s salt)

Verity and vast diversity in the preparation of coordination compounds have led to equally diversified applications in different areas They find uses as pharmaceuticals, polymeric products, paints, fungicides, analytical reagents, photo-conductors, petrochemical products, novel catalysts, anti-cancers, anti-oxidants and diagnostic imaging agents. The coordination compounds and the phenomenon of coordination flourish the nature by various life processes too. Chlorophyll, Hemoglobin, Vitamin-B complex, and many enzymes are coordination complexes.

A. TRANSITION METAL IONS AND THEIR COMPLEXES

Transition elements may be generally defined as those which as an element or as an ion have partially filled d or f sub-shells. However, in a broader sense, all those having partially filled *d* or *f* shells in any of their oxidation states will be treated as transition elements.

Based on their acceptor properties, the transition metal ions are classified in to two, Class ‘a’ and Class ‘b.’[11]. Class ‘a’ metals are hard acids and are usually cations of electropositive metals with high oxidation states, consequently they are relatively non-polarisable and have higher charge-to size ratio. Class ‘b’ behavior is associated with low or zero oxidation state, large size and polarizable outer electrons[12]. Class ‘a’ metal ions form their most stable complexes with donor atoms of the second period (N, O, F) and Class ‘b’ with donor atoms of third and subsequent periods of the periodic table.

Pearson considered Lewis acids with Class ‘a’ characters as ‘hard’ and those with Class ‘b’ characters as ‘soft.’ The terms hard and soft are relative, and as there is no sharp demarcation line between these two, a ‘broader line’ class also exists.[13,14]

Usually stable complexes are those derived from the interactions of soft acids with soft bases and hard acids with hard bases. For a verity of M(II) complexes of the first transition series, the stability order found is, Mn < Fe < Co < Ni < Cu > Zn. This is referred to as natural order of stability or Irving William`s stability order, which is consistent with the size of the M(II) ions.[15]

Oxidation sates below II: All metals form at least a few compounds in the oxidation states, I, 0, -I, but only with ligands of the π-acid type or π-complexing ligands. In this case of copper, insoluble binary Cu(I) compounds such as CuCl, CuBr, etc, are known. The complex compounds of Cu(I) are also known[15]. In the absence of complexing ligands, Cu(I) ion has only a transitory existence in water, although it is quite stable in acetonitril as $[Cu(MeCN)_4]^+$

Oxidation state II: All the elements from Ti to Cu form distinct binary compounds in the divalent state, such as oxides and halides, which are essentially ionic. Except for Ti, all the others form aqua ions of the type, $[M(H_2O)_6]^{2+}$. In addition, all these bivalent metal ions form a broad range of complex compounds, which may be cationic, neutral or anionic depending on the nature of the ligands[15].

Oxidation state III: All the elements form at least some compounds in this state. This is the highest oxidation state known for copper, in simple compounds and in complexes. The fluorides and oxides are again usually ionic, though the chloride may have significant covalent character, as in $FeCl_3$. All elements, from Ti to Co form aqua ions, although the Co(III) and Mn(III) ions are readily reduced in aqueous solution. Certain anions readily form metal(III) complexes in aqueous solution.

Oxidation state IV: This is the most significant oxidation state of Ti. TiO_2 and $TiCl_4$ are important compounds. It is also an important state for vanadium, which forms the vanadyl ion, VO^{2+} and many cationic, anionic, and neutral derivatives containing the VO species. For the remaining elements, Cr to Ni, the IV state is found mainly in flurides, fluro complex anions and cationic complexes. However, other important classes of compounds are the salts of the oxo ions and other oxo species.

Oxidation sates V, VI and VII: These oxidation states are found only for Cr(V and VI), Mn(V, VI and VII), Fe(V and VI) and Co(V). Apart from flurides (CrF_5 and CrF_6), oxoflurides (MnO_3F) are also stable. However, the main chemistry is that of the oxoanion; $M^nO^{(8-n)}$. All the compounds in these oxidation states are potent oxidizing agents.

1. Typical complexes of first transition metal ions

The uses and applications of transition metals and their compounds were known from the pre-scientific *era* itself. By complexation, their properties are customized in many appealing ways. Therefore, systematic studies on new complexes of transition metals have much importance.

The size of Se^{3+} is smaller than that of the other ions of the first transition series. It therefore, readily forms complex ions, as for example, $[SeF_4]^{3-}$, $[Se(bipy)_3]^{3+}$, $[Sc(DMSO)_3]^{3+}$, etc., where, bipy= bipyridyl and DMSO= dimethysulphoxide[33]. Some bidentate chelating agents such as $C_2O_4^{2-}$ in

$[Sc(C_2O_4)_2]^-$, and acac (acetyl acetone anion) in $[Sc(acac)_3]$, are also known to form chelates with Sc.$^{3+}$

The +2-oxidation state of titanium is not very stable. It has no aqueous chemistry because it is readily oxidised by water liberating hydrogen. The two important compounds formed by Ti(II) are TiO and $TiCl_2$. $TiBr_2$ and TiI_2 are also known[34]. The colorimetric estimation of TiO^{2+} or $[Ti(OH)_2]^{2+}$ in aqueous solution is carried out by the addition of H_2O_2 to the solution when an orange color is developed due to the formation of a peroxo complex of Ti^{4+} whose possible formula is $[Ti(O_2)OH.(H_2O_2)_n]^+$.[35-37]

The outer electronic configuration of vanadium is $3d^34s^2$. It shows oxidation states of +2,+3,+4 and +5 in its compounds.[38] The compounds in the lower oxidation states are good reducing agents. They are ionic in character and because of incomplete electron shells, they are also colored. One of the basic vanadium complex is $[V(H_2O)_6]^{2+}$ ion. Some other V(II) complexes are also known,[39] eg, $K_4[V(CN)_6]$ and $[V(en)_3]Cl_2$. The complexes of V(III), in general, are not very stable. Vanadium tetrachloride and- tetrafluride complexes of the types, VCl_4L and VF_4L2, where L stands for a unidentate ligand. These complexes are readily hydrolyzed to their hydroxides by water.[40,41]

Chromium forms a number of compounds in which its oxidation state is +2,+3 or +6. Cr(II) state is not very stable. However, some of the hydrated salts are stable,[42] eg. $CrCl_2.4H_2O$ and $CrSO_4.7H_2O$. Cr(II) acetate hydrate is known to exist in the form of a dimer[43]. Some complexes of Cr(II) such as $[Cr(NH_3)_6]^{2+}$ are relatively more stable than simple Cr(II) compounds.[44] The +3-oxidation state is highly stable in acidic medium but it is oxidized readily to +6 state in alkaline medium. Thus, Cr_2O_3 is oxidized to Na_2CrO_4 in alkaline medium. Trace amount of chromium is necessary in the diet of mammals. Cr(III) and insulin maintain the correct level of glucose in the blood. If Cr(III) is totally absent in the body, the removal of glucose from the blood would occur at lower rates than normal.[45]

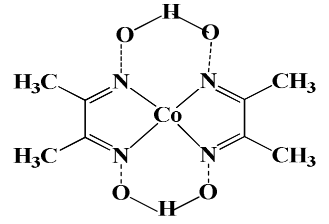
Complexes of Mn(II) are well known. Some of the hydrated salts, such as $Mn(ClO_4)_2.6H_2O$, contain the complex ion, $[Mn(H_2O)_6]^{2+}$ in which manganese is in +2 oxidation state[46,47]. The formation of hexamine ion, $[Mn(NH_3)_6]^{2+}$, by the direct action of ammonia on anhydrous salts of Mn(II) is also reported[47]. These complexes are octahedral and have pink colour. They have five unpaired electrons in *3d* subshell. Their magnetic moments, therefore, lie in the range of 5.8 – 6.1 BM. They are highly stable and resist attack by oxidizing- as well as reducing agents[48]. Several tetrahedral complexes of Mn(II) are also known. These, however, are not stable in aqueous solution and exist in solvents of low dipole moments such as chloroform, nitrobenzene, etc. Some examples of such complexes are tetra halo anions, $[MnX_4]^{2-}$, stabilized with large cations (e.g., R_4N^+, R_4P^+). The tetrahedral complexes show a greenish- yellow color. They have five unpaired electrons in the *3d* sub-shell and are, therefore, high-spin complexes with magnetic moments in the range from, 6.1 to 5.8 BM[49].

The common oxidation states of iron are +2 (ferrous) and +3 (ferric). Almost all the aqueous chemistry of iron is confined to the +2 and +3 oxidation states[50,51]. Iron(II) in aqueous solution exists as $[Fe(H_2O)_6]^{2+}$. This ion is pale green in color. Fe^{3+} ion forms even larger number of complexes than Fe^{2+} ion. In most of these, the coordination number of Fe^{3+} ion is six and the complexes formed are octahedral[52]. However, a few complexes in the coordination number four and with tetrahedral geometry are also known. $[FeCl_4]^-$ is the most important tetrahedral complex. The tetra-halo complexes of Fe(III) are particularly stable if the cation is bigger in size. Examples are $[(t\text{-}Bu)_4 N]^+[FeX_4]^-$, where X is Cl^- , Br^- or I^-.

Variety of octahedral complexes are known. Fe^{3+} ion has a strong tendency to form complexes with ligands which coordinate through oxygen, e.g., sulphate (SO_4^{2-})- and the oxalate ($C_2O_4^{2-}$) ions. The trioxalato complex, $[Fe(C_2O_4)_3]^{3-}$ is highly stable (that is why oxalic acid is used for removing iron stains from clothes). The hexaaquo ion, $[Fe(H_2O)_6]^{3+}$, is stable only in strongly acidic solution. However, the hexachloro- and hexacyanoferrate(III) complexes, i.e., $[Fe(Cl_6]^{3-}$ and $[Fe(CN)_6]^{3-}$, are known to be highly stable. These complex ions contain only one unpaired electron and are, therefore, low-spin[53].

Like iron, cobalt has two important oxidation states, +2 and +3. Cobalt(III) state is far less stable than Cobalt(II) state[54]. However, in basic solutions, oxidation of Co^{2+} to Co^{3+} takes place relatively easily. It can be kept exposed to air for an indefinite period. Co^{2+} ion, in water, exists in the hydrated state as $[Co(H_2O)_6]^{2+}$ and is pink in colour[55]. It turns blue when heated due to dehydration. Thus, the anhydrous Co(II) salts are blue in colour. It turns pink when hydrated. Anhydrous $CoCl_2$ added to silica gel is, therefore, used for testing moisture. Most of the cobalt(II) compounds are soluble in water[56]. When a base is added to a solution containing Co^{2+} ion, cobalt(II) hydroxide separates out as a blue precipitate. When cobalt(II) hydroxide is heated in the presence of air, mixed Co(II) –Co(III) oxide, Co_3O_4, is obtained. This oxide has a normal spinal structure with Co^{2+} ions in tetrahedral- and Co^{3+} ions situated in octahedral sites created due to cubic close packing (CCP) arrangement of the oxide ions[57]. Co(II) ion forms octahedral complexes such as $[Co(NH_3)_6]^{2+}$, tetrahedral complexes such as $[CoCl_4]^{2-}$. Planar complexes such as dimethylglyoximatocobalt(II) are also known[57]. (**Fig. 7**)

Fig. 7: dimethylglyoximatocobalt(II)



The outer electronic configuration of Ni is $3d^8 4s^2$. It shows the oxidation states of 0,-1,+1,+2,+3 and +4. The anion, $[Ni_2(CO)_6]^{2-}$ contains nickel in -1 oxidation state whereas $[Ni(CO)_4]$, $[Ni(PF_3)_4]$, $[Ni(PF_3)_2(CO)_2]$ and $K_4[Ni(CN)_4]$ contain nickel in zero oxidation state[58]. The +1 oxidation state of nickel is very rare. Nickel in +1 state is present in $K_4\,[Ni_2(CN)_6]$

For nickel, +2 state ($3d^8$) is the only stable oxidation state. A few compounds of trivalent nickel ($3d^7$) also known. They are very strong oxidizing agent. The stability of Ni in +3 and higher oxidation states decrease with increasing molecular mass[59,60]. Nickel(II) ion, is generally hydrated and exists as $[Ni\,(H_2O)_6]^{2+}$, green in colour. The salts of Ni^{2+} are green or blue[61].

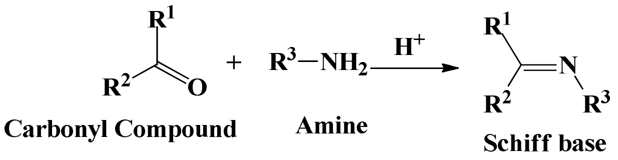
The outer electronic configuration of copper is $3d^{10} 4s^1$. It shows oxidation states of +1 ($3d^{10}$) and +2 ($3d^9$) in its compounds, and known commonly as cuprous and cupric compounds, respectively[62,63]. The +1 oxidation state of copper is not stable. In Cu(I), the *d* orbitals are completely filled and the electrons are fully paired and Cu(I) compounds are, therefore, diamagnetic. Copper(I) ion in solution changes readily to copper(II) ion[64]. The aqueous chemistry of copper in +2 oxidation state is similar to that of the +2 ions of the other transition elements. Although most of the anhydrous copper(II) salts are colorless, they are blue when hydrated[65]. This is due to the presence of hydrated ion, $[Cu(H_2O)_4]^{2+}$ which is blue[66].

Zinc shows +2 oxidation state in all of its compounds and are colourless. It undergoes slight hydrolysis in water giving acidic solution[67]. The oxidation potential for this half reaction is 1.22 volts, while that in acid solution is only 0.76 volts. This shows that zinc metal acts as a stronger reducing agent in alkyne solution than in acid solution[68]. As already mentioned, Zn^{2+} ion forms a number of complexes, like the divalent ions of other transition elements[69,70]. Zn^{2+} ion is hydrated in solution, yielding the complex ion, $[Zn(H_2O)_4].^{2+}$ Thus, a solution of zinc chloride in water may be written as $[Zn\,(H_2O)_4]Cl_2$.

B. SCHIFF BASES

Schiff bases are known since 1864 when Hugo Schiff synthesized and reported the condensation product of primary amines with carbonyl compounds[71]. Compound containing an azomethine group (-CH=N-), known as Schiff base is easily formed by the condensation reaction of a primary amine with a carbonyl compound (aldehyde or ketone)[72-77]. Schiff bases of aliphatic aldehydes are relatively unstable and are readily polymerized while those of aromatic aldehydes, having an effective conjugation system, are more stable[78]. Some people restrict the term, Schiff base to secondary aldimine (azomethine where the carbon is connected to a hydrogen atom), thus with a general formula, RCH=NR'. The chain on the nitrogen makes the Schiff base a stable imine[79-85]. A Schiff base derived from aniline, where R^3 is a phenyl-or a substituted phenyl radical, can be called an anil[86-89]. (**Scheme. 1**)

Scheme. 1: Preparation of Schiff bases



R^1 & R^2 = H, $-CH_3$, -Ar, R^3 = $-CH_3$, -Ar

Schiff bases have coordination sites ranging from one to seven,[90,91] and may be monodentate, bidentate (N-N[92,93] -or N-O donors[94]), tridentate[95,96] or polydentate ligands.[97,98] In a monodentate Schiff base, it has been noted that the basic strength of the C-N group is not sufficient to obtain a stable complex by the coordination of imino nitrogen atom to a metal ion.[99] Hence, the presence of at least one more additional donor atom, suitably oriented near the N stabilizes the metal-nitrogen bond through the formation of five- or six membered chelate ring.

Schiff base could be applied in different areas such as separation processes, metallic deactivation, bioinorganic chemistry, catalysis, electro chemistry and environmental chemistry.[100,101] Microwave assisted preparation of a series of Schiff bases by efficient condensation of salicylaldehyde and aryl amines without solvent is described as a high yield and an environmentally friendly method in organic synthesis[102]. Schiff bases find applications in the field of agriculture (as pesticide) and in medicine with their highly effective antibacterial and anticoagulant activities.[103]

Schiff base complexes continue to attract many researchers because of their wide applications in various industrial, analytical and pharmaceutical fields.[104,105] Schiff bases also have a number of applications in analytical chemistry *ie*., synthesis, identification, detection and determination of aldehydes and ketones. They are also used in the purification of carbonyl- and amino compounds and protection of these groups during complex- or sensitive reactions. They form the basic units in certain dyes. In organic synthesis, Schiff base formation reactions are useful in making carbon-nitrogen bonds. Schiff base appears to be an important intermediate in a number of enzymatic reactions involving the interaction of an enzyme with an amino- or a carbonyl group on the substrate[105-115]. One of the most important types of catalytic mechanism in the biochemical process is that which involves the condensation of a primary amino group of an enzyme, usually that of a lysine residue, with a carbonyl group on the substrate to form an imine[116-124].

1. **Applications of Schiff base ligands and their complexes – a brief review**
    a. **As catalysts**
    b. **Biological applications**
    c. **Miscellaneous applications**

Nowadays, the research field dealing with coordination chemistry of Schiff bases has expanded enormously.[125-137] The importance of Schiff base complexes in bioinorganic chemistry, biomedical applications, supramolecular chemistry, catalysis, material science, separation and encapsulation processes and formation of compounds with unusual properties and structures has been well recognized and reviewed[138-146]. Their preparation, various physico-chemical properties and important applications in industrial- biological- and medical fields have already been discussed in detail in the standard texts and literatures[147-155].

a. As catalysts

Abolfazl[156] synthesized a new Schiff base vanadyl complex of N, N 0 -bis(5-[(triphenylphosphoniumchloride)-methyl-salicylidine)meso-stilben-diamine)] and immobilized it on a solid support, sodium montmorillonite[156]. This complex acts as a good catalyst in the epoxidation of olefins using tert-butylhydroperoxide in acetonitrile. Here the supported vanadyl complex shows 100 % selectivity for epoxidation with a 98 % conversion for cyclohexene. It can be reused four times without any reduction in the catalytic properties.

M. Kooti *et. al*[157] reported new silica-coated cobalt ferrite nanoparticles and functionalized them with Schiff bases to get immobilized bidentate ligands. The new functionalized magnetic nanoparticles were then treated with $Mo(O_2)_2(acac)_2$, resulting in a novel immobilized molybdenum Schiff base catalyst. It was characterized by X-ray powder diffraction, vibrating sample magnetometry, thermogravimetric analysis, transmission electron microscopy, FT infrared- and inductively coupled plasma atomic emission spectroscopy. The immobilized Mo complex was shown to be an efficient heterogeneous catalyst for the oxidation reactions of various alkenes using *t*-BuOOH as oxidant.

A special catalytic application of the Schiff base complex was reported by M. Nikpassand *et. al*[158]. IR- and NMR spectra and elemental analysis, were used to characterize the compounds. They introduced a facile and suitable procedure for the synthesis of diindolylmethanes in a small reaction time and high yields using the newly synthesized complex as an efficient recyclable heterogeneous catalyst.

Mohsen Nikoorazm *et. al*[159]. Synthesized and characterized an efficient and highly selective heterogeneous catalyst, Cu(II) Schiff base complex and immobilized it on mesporous MCM-41. This heterogeneous catalyst showed excellent catalytic efficiency in the oxidation of various sulfides and thioles in the presence of urea/hydrogen peroxide. It could be reused for at least four cycles without any significant loss in the activity.

Zamanifar *et. al.*[160] synthesized and characterized a vanadium complex of N-salicylidene- L -histidine and immobilized on Al-MCM-41 and designated it as VO(Sal-His)/Al-MCM-41. The Schiff base complex was characterized by X-ray powder diffraction (XRD), FT-IR, nitrogen adsorption–desorption and chemical analysis techniques[160]. The new complex was found to catalyze the epoxidation of *trans*-2-hexen-1-ol, cinnamyl alcohol and geraniol in presence of *tert*-butyl hydroperoxide. As a successful catalyst, VO(Sal-His)/Al-MCM-41 showed with 99% conversion and high selectivity in these reactions.

Zhang *et.al*[161] synthesized a novel Mo(VI) Schiff base complex and modified it to hybrid heterogeneous catalysts by the reaction with mesoporous SBA-15. It was then functionalized by the grafting procedures using 3-aminopropyl-triethoxysilane and salicylaldehyde. The catalytic activity could be further enhanced by silylation using Me_3SiCl. The catalytic activity of the hybrid material was further investigated under various reaction conditions. The Mo–CH_3–SA–NH_2–SBA-15-catalyst can be recycled efficiently and reused in four cycles with significant activity.

A novel Schiff base, N-(phenolyl)-benzaldimine (HL) and its V(IV) complex of the general composition, $[VO(L)_2]$, where L = 1⁄4O, N donor of

Schiff base, were synthesized by Mojtaba Bagherzadeh *et. al*[162]. The complex was then characterized by elemental analysis, molar conductance data, FT-IR, H^1- and C^{13}-NMR, and UV-Vis spectroscopic techniques. This complex catalysis the oxidation of various alcohols to aldehydes and ketones using ozone as oxidant. The reaction was carried out in a biphasic reaction condition ($CH2Cl_2/H_2O$) with the help of a phase transfer agent, tetra-n-butylammonium bromide in air at room temperature.

Akbar Mobinikhaledi *et.al*[163] synthesized a new complex, Cu(II)-2,20-[{(methylenebis-(oxy)*bis*-(2,1-phenylene))*bis*-(azanylylidene)}*bis*-(methanylylidene)]diphenol. It was encapsulated in the supercages of zeolite NaY by the flexible ligand method. The resulting products were completely studied and characterized by various physico-chemical and spectral methods. The free complex and the encapsulated one were used as catalysts for the synthesis of benzimidazole. The results showed that the catalytic activity and stability of the complex were increased by encapsulation. The effects of amount of catalyst, solvent, leaching and reusability of the heterogeneous catalyst were investigated.

b. Biological applications

Sohan Lal *et.al*[164] reported a series of Schiff bases of chitosan. They were prepared by condensation reaction of different aromatic aldehydes with chitosan. Their structures were elucided by elemental analysis (C, H, and N), FT IR- and ^1H NMR spectroscopy. The ^1H NMR spectroscopy was mainly used to determine the degree of deacetylation of chitosan and the degree of substitution. The thermogravimetric studies of Schiff base polymers showed that they have nearly the same decomposition temperature as that of the chitosan. The antimicrobial properties of chitosan and its Schiff bases were tested against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Aspergillus niger* and found that the Schiff bases of chitosan were more active than chitosan.

A special biological application of Schiff base complexes was reported by K. Singh *et.al*[165]. The organotin(IV) complexes having the formulae, $R_2MCl[L]$ and $R_2M[L]_2$ were synthesized by the reactions of Me_2MCl_2 with Schiff bases, [5-Mercapto-4-(pyrrolcarboxalideneamino)-s-triazole, 5-Mercapto-3-methyl-4-(2-pyrrol-carboxalideneamino)-s-triazole and 3-Ethyl-5-mercapto-4-(pyrrolcarboxalideneamino)-s-triazole] in 1:1 and 1:2 molar ratios. The ligands and complex were characterized by elemental analysis, molar conductance, IR, UV, ^1H-, C^{13}-and Sn^{119}-NMR spectral techniques. The IR- and H^1 NMR spectral studies suggested the participation of azomethine nitrogen in the coordination with the central metal atom. With the help of the above mentioned spectral studies, penta -and hexa coordinated environments around the central metal atoms in the 1:1 and 1:2 complexes, respectively, have been proposed. Finally, the free ligands and their metal complexes were tested *in vitro* against some pathogenic bacteria and fungi to assess their antimicrobial properties. They showed an excellent activity against the tested microbial organisms.

Bagihalli *et.al*[166] synthesized a series of novel complexes of Zn(II) with biologically active 1,2,4-triazoles Schiff bases derived from the condensation of three substituted 4-amino-5-mercapto-1,2,4-triazole with 8-formyl-7-hydroxy-4-methylcoumarin. The Schiff bases and their complexes have also been screened for their antibacterial activities against *Escherichia. coli, S. aureus, S. pyogenes, P. aeruginosa* and *Salmonella typhi* and antifungal activities against *Aspergillus niger, Aspergillus flavus* and *cladosporium* by MIC technique.

A swift method using microwave irradiation has been developed by Yongle Peng *et. al*[167]. for the synthesis of a novel Schiff base, 4-amino-3-[3-(1-benzyl)indole]-5-thiomethyl-1,2,4-triazole and its derivatives. The distinctive advantages of the method are a little reaction time and good conversion. The ligand was characterized based on their elemental analysis, IR, H^1 NMR and mass spectral techniques. The antibacterial action of the ten novel Schiff bases against three bacterial strains was studied by the disk diffusion method. Preliminary results indicated that some of the compounds have good antibacterial activity.

A series of novel metal complexes of the Schiff base, 2-[(E)-1*H*-1,2,4-triazol-3-ylimino)methyl]phenol) were synthesised and characterised by Larisa Calu *et. al*[168]. The characteristics of the compounds have been assigned from micro analytical, magnetic and thermal data as well as by IR, UV–Vis, ^{1}H NMR and EPR spectroscopy as well as magnetic data at room temperature. The electrochemical behaviours of the complexes were investigated by cyclic voltammetry. The TG/DTA analysis of these complexes in flowing air indicated the occurrence of water molecule in the complexes as well as the oxidative degradation of the Schiff base. Powder X-ray diffraction studies indicated that the final product of decomposition was the most stable metal oxide. The complexes showed enhanced antibacterial activities in comparison with the ligand towards both *planktonic* as well as bio-film embedded cells. The Cu(II) and Zn(II) complexes exhibited inhibitory effect on the tumour cell lines growth, as revealed by the amplified G2 phase and percentage of *apoptotic/necrotic* cells.

Raman *et.al*[169] synthesized a novel tetra dentate N_2O_2 Schiff base by the condensation reaction between 1-phenyl-2,3-dimethyl-4-aminopyrazol-5-one(4-aminoantipyrine) and 3-salicylidene-acetylacetone. The stable complexes of the first transition metal ions, Co(II), Ni(II), Cu(II) and Zn were also prepared. Micro analytical data, magnetic susceptibility, IR, UV-Vis, ^{1}H-NMR, ESR and Mass spectroscopic techniques were used to corroborate their structures. Electronic absorption spectra of the complexes put forward a square-planar geometry around the central metal ion. These complexes showed higher conductance values, supporting their electrolytic nature. The monomeric nature of the complexes was established from their magnetic susceptibility values. Cyclic voltammograms of the Cu(II) and Ni(II) complexes in DMSO solution at 300 K were recorded and the results were discussed. The X-band ESR spectrum of the copper complex was recorded and the molecular orbital coefficient values were calculated from the spectrum. The *in vitro* antimicrobial activities of the complexes were tested against bacteria such as *Klebsiella pneumoniae, Staphylococcus aureus, Bacillus subtilis* and *Escherichia coli* and fungi like *Aspergillus niger* and *Rhizoctonia bataicola*. Majority of the metal chelates exhibited higher antimicrobial activities against these microorganisms than the free ligand.

Mendu *et. al*[170] synthesized a series of Cu(II) , Ni(II) , Co(II) , Mn(II) and Zn(II) complexes of Schiff base, 4-chloro-2–((4-oxo-4H-chromen-3yl) methylene amino) benzoic acid (L). Based on various physico-chemical measurements, especially, elemental analysis, conductance measurements and spectral studies, 6-coordinate geometry was assigned to these metal complexes. The ligand, L behaved as a tridentate one and coordinated through the nitrogen atom of azomethine group, O^- of the carboxyl group and oxygen atom of keto group of γ-pyrone ring. The interaction of Cu(II) complex with CT- DNA was carried out by UV–Vis, fluorescence titrations and viscosity measurements. The metal complex binds to DNA through intercalative binding mode. The biological activites have been studied on four bacterial strain, *E.coli, B.subtilis, pseudomonas* and *Edwardella* and two fungi *penicillium* and *trichoderma* by disc diffusion technique and established that the metal complexes were moderately active than the free ligand.

A special biological application of Schiff base complexes was reported by B. Anupama *et.al*[171]. Complexes of Co(II), Ni(II), Zn(II), Fe(III) and VO(II) have been prepared with the Schiff base, 2,3-dimethyl-1-phenyl-4-(2-hydroxy-3-methoxy benzylideneamino)-pyrazol-5-one (L), obtained by condensation of 4-aminoantipyrine with 3-methoxy salicylaldehyde. Quenching studies of the Schiff base metal complexes indicated that they powerfully bind to DNA. Viscosity measurements pointed out that the binding mode of the metal complexes with CT

DNA was by intercalation through groove. The ligand and its complexes were screened for their antibacterial activities against bacteria. The article summarized that the above mentioned metal complexes were biologically active, while the ligand was not.

Transition metal complexes of the type, $[NiL_2Cl_2]\cdot H_2O$ and ML_2Cl_2, where M = Co(II), Cu(II), Cd(II), Zn(II) or Hg(II)] and L = Schiff base, prepared from the condensation of naphthofuran-2-carbohydrazide and 2-chloro-3-formylquinoline have been synthesized and reported by M. B. Halli *et. al*[172]. The free ligand and its metal complexes have been analyzed for their *in vitro* antibacterial and antifungal activities by minimum inhibitory concentration method (MIC). The influence of all the complexes towards DNA cleavage activity was evaluated by agarose gel electrophoresis method. The free ligand and its complexes have been studied for their antioxidant action by DPPH method. The results of bioassay have shown that the metal complexes were active than the free ligand.

Nursen Sari *et. al*[173] investigated the antibacterial and antifungal activities of novel D-amino acid Schiff bases and their Cr(III) and Ni(II) complexes. All these complexes have been examined against pathogenic strains, *Listeria monocytogenes 4b* ATCC19115*, Staphylococcus aureus* ATCC25923, *Escherichia coli* ATCC1280, *Salmonella typhi H* NCTC 901.8394, *Brucella abortus* (A.99, UK-1995) RSKK03026, *Staphylococcus epidermis sp., Micrococus luteus* ATCC9341, *Shigella dysenteria typ* 10 NCTC 935 and *Candida albicans* Y-1200-NIH. The results indicated that the complexes exhibited better activities than some antibiotics available in the market. In particular, diamagnetic Ni(II) complexes were more potent bactericides than all of the bactericides available in the market.

Genc *et.al*[174] reported a series of novel Ni(II), Cu(II) and Zn(II) complexes of the Schiff bases derived from terphthaldehyde with 4-aminobenzoic acid and amino acids (glycine, β-alanine). The cytotoxic activities of the complexes against human breast carcinoma, MCF-7 cell line have been studied. Ligands and their Zn(II) complexes inhibited cell proliferation of MCF-7 cancer cell lines in a dose- and time-dependent manner. The free radical scavenging activities of the complexes were measured using 1,1-diphenyl-2-picryl-hydrazil (DPH) as a standard. The results showed that these complexes induced oxidative damage by raising the lipid peroxidation since Malondialdehyde (MDA) formation was increased. However, the antioxidant activities of the compounds were very much lower than those of the standard antioxidants.

A new series of antibacterial and antifungal triazole derived Schiff base ligands have been prepared by Sajjad. H Sumrra *et. al*[175] by the condensation reaction of 3,5-diamino-1,2,4-triazole with methyl-, chloro- and nitro-substituted thiophene-2-carboxaldehydes in 1:2 molar ratio. These Schiff bases made to react with $VOSO_4 \cdot 5H_2O$ in (1:2) (metal:ligand) molar ratio. All the VO(II) complexes were assigned square-pyramidal geometry. The *bio-assay* results, especially, *in vitro* antibacterial and antifungal data showed that the complexes were more potent antibacterial- and antifungal agents than the parent Schiff bases ligands.

c. Miscellanious applications

Aiad[176] reported an important analytical application of complexes of Schiff base derived from the condensation reaction of diethylenetriamine with benzaldehyde and anizaldehyde. These compounds were tested as surfactants. A variety of surface properties, mainly, effectiveness, efficiency, critical micelle concentration, maximum surface excess and minimum surface area of the ligand and its metal complexes were evaluated. These surfactants were evaluated for their corrosion inhibition properties. Their antimicrobial actions against gram-positive and gram-negative bacterial strains were also evaluated. The results showed that they were better emulsifiers and filter loss control agents for oil-base mud. It was estimated that they have good corrosion inhabitation ability for low carbon steel alloys and good bactericidal effect.

Soltani *et. al.*[177] reported the corrosion inhibition of low-carbon steel in HCl by N, N, O-bis(salicylidene) benzidine (Schiff base A) and bis(5-nitrosalicylidene) benzidine (Schiff base B). The experimental techniques used in the study were chemical (weight-loss)- and electrochemical potentiodynamic polarization- and electrochemical impedance spectroscopic (EIS) measurements. Polarization curves disclosed that these Schiff bases were mixed-type inhibitors. Results showed that the inhibition efficiency increased when the inhibitor concentration increased. The inhibition efficiency followed the order, Schiff base B > Schiff base A. The experimental data exactly fitted with Langmuir adsorption isotherm. The activation- and thermodynamic adsorption parameters were also calculated and discussed. Quantum chemical calculations were performed to theoretically describe the relationship between molecular structure and inhibition efficiencies of these Schiff bases.

Two series of Schiff bases were prepared by the condensation of benzaldehyde and anisaldehyde with three fatty amines having different alkyl chain lengths, ie, dodecyl-, hexadecyl- and octadecyl amines[178]. Based on the analytical data, the purity and probable structures of these Schiff bases and complexes were established. The Schiff bases were evaluated as corrosion inhibitors for low carbon steel (mild steel) in various acidic media (HCl and H_2SO_4) using weight loss method. The data showed that these inhibitors have high protection of the low carbon steel alloys against corrosion process in the tested acidic media.

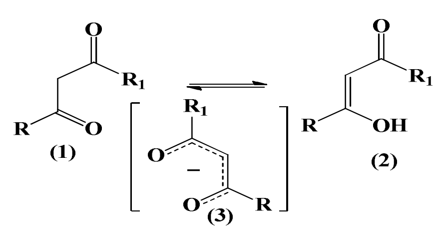
Manawadevi *et. al*[179] reported the applicability of simple Schiff base transition metal complexes, [M(L)], where M = Ni(II) or Cu(II) and L = N, N, O-ethylenebis(acetylacetoniminate), as sensing materials and indicators in qualitative, spectroscopic and volumetric determinations of acids and bases. Acid-base titrations can be carried out using these complexes as indicators. Alcoholic solutions of [Cu(L)] and [Ni(L)] were purple and orange-red, respectively, and both solutions become colourless upon adding strong acids.

A special analytical application of Schiff base complexes was reported by S. Sahrokhin *et. al*[180]. The electrochemical oxidation of thiocytosine on the surface of carbon-paste electrode by the Schiff base (salophen derivatives) complexes of cobalt was studied. Co(II)-5-nitrosalophen, because of its electrophilic functional group, led to a significant improvement in the catalytic action, sensitivity (peak current) and a noticeable increase in the anodic potential of the modified electrode. The electrode showed an extremely good reproducibility and high stability in its voltammetric response.

2. Schiff base complexes derived from active methylene compounds.

If a methylene (-CH_2-) group or substituted methylene (-RCH-) group is interposed between two alkyl- or aryl- groups in a compound, it is termed as ‘active methylene compound. **(Fig. 8)**

Fig. 8: keto–enol tautomeric forms

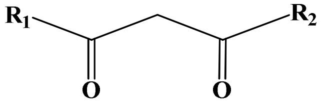


Since the H atoms present on the methylene group are always activated by the adjacent carbonyl (carboxyl/ester, etc.) groups or a conjugated system, a phototropic shift leading to a keto (1) and enol (2) tautomerisation occurs. The amount of enol tautomer dependents on a verity of factors such as solvent, temperature, substituent groups at 1, 2 positions and the H-bonding species present. Bulky alkyl substituent on the second carbon leads to a decrease in the amount of enol content, while the groups such as, Cl, Br, CN, COOH, SCH_3, etc. lead to almost 100% of enolization. If halogen atoms substitute both the H atoms at α position, the enolisation will be suspended[185].

The methilinic proton in the keto form and hydroxyl proton in the enol form are acidic. The removal of any of this H atom generates the 1,3-diketone anion (3) which is the source of a broad class of coordination compounds referred to as 1,3-diktonates. The enol contents in acetoacetanilide and ethylacetoacetate are low. It is due to the involvement of N- and O lone pairs diminishing the electron density on the carbonyl carbon.[186]

Typical active methylene compounds that are able to couple with diamine include the following types (**Table. 9 & Table. 2**)

Fig. 9: Activemethyline compound



R_1 & R_2 = alkyl or Aryl etc.

Table. 2: Type of compound Activemethyline compounds

R_1	R_2	Type of compounds
Alkyl / aryl	Alkyl / aryl	1,3- diketone
Alkyl	Alkoxy / aryloxy	β-diketoester
Alkyl	-OH	β –ketoacid
Alkyl / aryl	-NH Ph	β-ketoanilide

A large number of multidentate- and macrocyclic Schiff base ligands can be synthesized by the condensation reaction between active methylene compounds and diamines. These ligand systems have evoked considerable interest because of their utility as model compounds in bioinorganic chemistry and in analytical studies.[187-189]

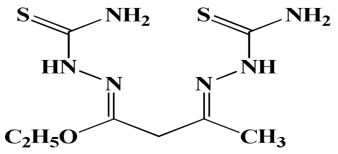
A novel Schiff base, (L) was synthesized by Rafet M. El-Shazly *et. al*[190] by the simple condensation between the two molecules of ethylacetoacetate and one molecule of ethylenediamine. Complexation of this ligand with copper(II) chloride gave poly-nuclear copper complexes of the type, Cu_3LCl_6, Cu_4LCl_8, Cu_5LCl_{10}, Cu_6LCl_{12}, Cu_7LCl_{14} and Cu_8LCl_{16}. Elemental analyses, molar conductivity and magnetic susceptibility measurements, X-ray powder diffraction and IR spectral studies have been used to characterize the above complexes. The IR spectra showed that the Schiff base bound in a tetradentate manner. The spectral and magnetic susceptibility measurements suggested the presence of a chlorine bridge between the Cu(II) ions. The magnetic susceptibilities of the complexes followed the Curie-Weiss law.

T. F. Zafiropoulose reported a new Schiff base ligand, diethyl(ethylenebis-β-aminocrotonate), (LH_2), that reacts with lanthanide(III) chlorides and -nitrates in various solvents to give solid complexes of the stoichiometries. They were characterized by conductivity measurements, X-ray powder patterns, thermal decomposition studies, magnetic measurements and spectral studies (IR, ^{1}H-NMR and electronic diffuse reflectance and solid-state emission f-f spectra).[191]

R. C. Mourya[192] reported four new mixed-ligand complexes of Mn(II). The composition of the complexes were $[Mn(pa)\text{-}(L)(H_2O)]$, where paH = picolinic acid and LH = acetoacetanilide (aaH), *o*-acetoacetanisidide (o-aansH), *o*-acetoacetotoluidide (o-aatdH) or ethylacetoacetate (eacacH). The complexes obtained have been characterized based on elemental analyses, molar conductance- and magnetic measurements, thermo gravimetric analysis, mass-, EPR-, infrared- and electronic spectroscopic studies. These novel complexes have shown significantly greater antibacterial activities against *Escherichia coli* and *Vibrio cholera* than the ligands. The 3D-molecular modelling and analysis for bond lengths and bond angles have also been carried out for a representative compound, $[Mn(pa)(aa)(H_2O)]$, to substantiate the anticipated structures.

S. El-Tabl *et. al*[193] reported the cytotoxic behavior and spectroscopic characterization of metal complexes of ethylacetoacetate *bis*-(thiosemicarbazone) (**Fig.9**). Cr(III), Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) formed mono- and binuclear complexes with this ligand. These complexes have been characterized by elemental analyses, IR- and UV–Vis spectra, magnetic moments, molar conductances, ^1H NMR- and mass spectra (ligand and its Zn(II) complex), thermal analyses (DTA and TGA) and ESR measurements. Based on spectral studies, octahedral or tetrahedral geometries have been assigned to the metal complexes. The complexes have been tested *in vitro* against tumor cells and a number of microbes in order to assess their antitumor and antimicrobial properties, respectively.

Fig. 9. Ethylacetoacetate *bis*-(thiosemicarbazone)

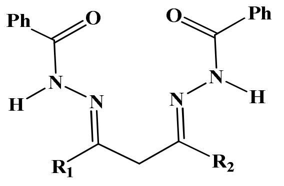


Novel mononuclear Ru(III) Schiff base complexes of the type, [RuX2(EPh3)(L)] (X = Cl or Br; E = P or As and L = monobasic tridentate Schiff base derived from o-aminophenol or o-aminothiophenol with ethylacetoacetate or ethylbenzoylacetate) have been reported by N. Sathya *et. al*[194]. The ligands coordinated to ruthenium through O, N, and O/S by dispropanation of the phenolic /thiophenolic group forming chelate rings. The structures and properties of the complexes were elucidated by various physico-chemical and spectral methods. Cyclic voltammetric data of all the complexes showed that the Ru(III)/Ru(IV) oxidation and Ru(III)/Ru(II) reductions within the range of 0–1.5

V, respectively, with respect to Ag/AgCl. Its applications as catalyst in the oxidation of alcohols using molecular oxygen at ambient temperature and in C–C coupling reactions were studied.

New tetradentate Schiff base ligands, derived from the condensation of benzoylhydrazide with dibenzoyhnethane (H_2L_l), benzoylacetone (H_2L_2) and thenoyltrifluoroacetone (H_2L_3) where reported by M. H. Attari *et. al*[195]. Their complexes were characterized based on elemental analyses, conductivity- and magnetic susceptibility measurements and using UV-visible-, infrared- and 'H-NMR- spectral data. Based on the mass spectra and elemental analyses, the complexes were assigned as; $[M(H_2L)C_{12}].nH_2O$ and $[M(L)].nH_2O$, when the compositions, where, M = Co(II)/Ni(II)/Cu(II), n = 0 to 5 and when M = Co(II)/Ni(II)/Cu(II), n = 0. **(Fig. 10)**

Fig. 10: benzoylhydrazide

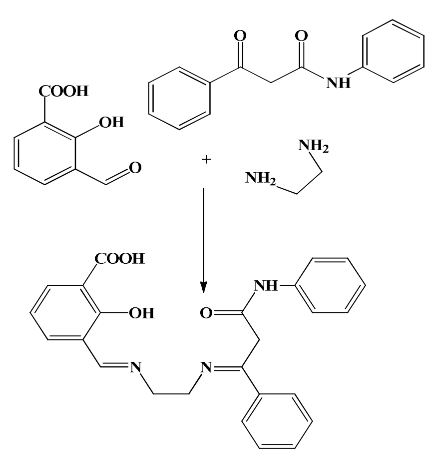


1. $R_1 = R_2 = Ph$, H_2L_1
2. $R_1 = -CH_3$, $R_2 = Ph$, H_2L_2
3. $R_1 = -C_4H_3S$, $R_2 = -CF_3$, H_3L_3

D. Kumar, *et. al*[196] reported novel polystyrene-anchored Cu(II), Zn(II), Cd(II), Ni(II), Mn(II), MoO_2(II), UO_2(II), Fe(III) and Zr(IV) complexes of an unsymmetrical dibasic tetradentate ONNO donor Schiff base derived from the condensation of chloromethylated polystyrene, 3-formylsalicylic acid, ethylenediamine and 2-benzoylacetanilide (PS–LH_2). (**Scheme.2**). Complexes have been characterized based on their elemental analysis, IR– and ESR spectra, and magnetic susceptibility measurements. Ni(II) and Cu(II) complexes were found to be square pyramidal and diamagnetic. Zn(II) and Cd(II) complexes were found to be tetrahedral. The Mn(II) and Fe(III) complexes were paramagnetic,

MoO_2(II) and UO_2(II) complexes were diamagnetic and Zr(IV) complex was diamagnetic and had pentagonal bypyramidal structure. All the other complexes were found to be octahedral in geometry.

Scheme. 2. Preparation of Ligand PS-LH_2



M. B. H. Howlader, *et.al*[197] reported interesting novel Schiff base complexes of the type, N,N′-ethylene-*bis*-(isonitrosoethylacetoacetateimino) M(II), where, M = Ni, Cu, Co, Mn, Zn or Cd. The complexes were synthesized by the reaction of diethyl ethylene- *bis*- (β-aminocrotonate) with metal acetates in presence of $NaNO_2$ in acidic medium. The starting material, diethyl ethylene - *bis*- (β-aminocrotonate), rearranges to N,N′- ethylene - *bis*-(isonitrosoethylacetoacetateimine) H_2L, which further releases two protons in the presence of transition metal ions forming metal complexes of the type, [ML]. The anticipated structures of the Ni(II) and Cu(II) complexes were square-planar. The Co(II) and Mn(II) complexes were octahedral and Zn(II) and Cd(II) complexes were found to be tetrahedral.

3. Schiff bases derived from vanillin

A novel vanilline derived Schiff base was reported by G. Hemakanthi, *et* *al*[198]. The stable monolayers of the Schiff base of o-vaniline have been formed at the air/water interface and on a sub-phase containing Cu^{2+}, Ni^{2+} and Zn^{2+} ions. Polarized UV–Visible spectra of the Langmuir–Blodgett (LB) films of the pure Schiff base and those of the metal complexes on solid substrates have been studied. The LB films pointed out that the aromatic rings in the polar plane were oriented slightly out of plane to the solid substrate. The orientation remained nearly the same for the ligand and the complexes. Low angle XRD indicated that the copper(II) complex and the ligand stacked into multimeric structures and their monolayers were compressed on the water surface.

O. V. Kotova reported the synthesis and photoluminascent activities of tetradentate Schiif base ligands derived from the derivatives of o-vanilline and ethylenediamine[199] and their Zn(II) complexes. The complexes were prepared by the reaction of ligand with $Zn(AcO)_2{\cdot}2H_2O$ in methanol at room temperature or under reflux. The complexes of composition, $ZnL{\cdot}H_2O$ were isolated irrespective of the temperature.

Complexes of *f*-block metal nitrates with Schiff bases derived from o-vanillin and 2-naphthylamine have been synthesized by L. Guofa, *et al.*[200] The complexes were assigned the general formula, $[LnL_2(NO_3)]\,(NO_3)_2$; where Ln = La, Ce, Pr, Nd, Sm, Eu, Tb, Dy, Ho, Er, Tm, Yb or Lu and L = Schiff base. The complexes were characterized based on their elemental analyses, molar conductance, IR and UV-Vis spectra and thermal analysis.

G. Zhong *et.al*[201] reported novel glycine-vanillin Schiff base metal complexes. Zn(II) and Ni(II) complexes of glycine–vanillin Schiff base were synthesized by one-step solid–phase reaction at room temperature. The complexes were characterized based on their elemental analyses, Fourier transform infrared spectra (FTIR), X-ray powder diffraction (XRD), and thermogravimetry and differential scanning calorimetry (TG–DSC). The experimental results pointed out that the Zn(II) and Ni(II) complexes were found to be six-coordinated octahedral. The antimicrobial study indicated that the two complexes had an intense antibacterial activity against *Escherichia coli*.

It was reported by Y. Zhang *et.al*[202] that the Mg(II) complex of the Schiff base derived from vanillin and L-tryptophan could bind with herring sperm DNA[202]. The binding properties between them in physiological pH environment (pH 7.40) have been studied by spectroscopic, cyclic voltammetric and viscosity methods. The resultant thermodynamic parameters proposed that the interaction between Mg(II)L and DNA was driven mostly by entropy. The results of the studies indicated that the mode of interaction between Mg(II)L and DNA were mainly electrostatic.

Mixed ligand Cu(II) complexes of the Schiff base derived from *o*-vanillin and l-tryptophan were prepared and characterized using conventional and spectroscopic techniques by L. Subha, *et al*[203]. Single crystal X-ray crystallographic studies showed that the Cu(II) was coordinated through N_2O_2 donors in a square planar manner. The EPR spectra of some of the complexes in frozen solution supported their square planar structures. Electrochemical behaviours of the complexes have been studied by cyclic voltammetry. The ligand and copper complexes exhibited cytotoxic action against MCF-7 cell line.

Wen Wu, *et. al*[204] reported a novel Schiff base derived from o-vanillin and o-phenylenediamine and its Zn(II) metal complexes. Complexes were prepared by the interaction of zinc acetate with the ligand in ethanol. The complexes were characterized based on their elemental analysis, IR- and fluorescent spectra (PL) and TG. Its antioxidative property was also studied. The fluorescence spectra of the Zn(II) complexes showed that excitation of the solid sample at 380 nm produced a strong emission with the peak maximum at 596 nm. The ligand exhibited a distinctive emission peak at 550 nm.

4. Schiff bases derived from *o*-hydroxyacetophenone

Novel Schiff base complexes of trichloro(cyclopentadienyl)titanium(IV) having the general formulae $CpTiCl_3SB$ and CpTiCl(SB'); where SB=Schiff bases derived from thiocarbohydrazide and benzaldehyde, *m*-nitrobenzaldehyde, *p*-nitrobenzaldehyde, acetophenone, *p*-hydroxyacetophenone, anisaldehyde, cinnamaldehyde or vanilline; $SB'H_2$=Schiff bases derived from thiocarbohydrazide and salicylaldehyde, or o-hydroxyacetophenone, have been synthesized and reported by Pandey *et. al.,* by the reaction of Schiff base with trichloro(cyclopentadienyl)-titanium in anhydrous dichloromethane[205]. The complexes were characterized by elemental analysis, electrical conductance, magnetic measurements and spectral (electronic, IR and ^1H NMR) studies. ^1H NMR spectra pointed out that there was fast rotation of the cyclopentadienyl ring around the metal-ring axis at 25°C.

Interesting novel polymeric metal complexes were reported by Narang *et. al.*[206] The polymeric complexes of the type, M_2L, where M = Cu(II), Ni(II) or Co(II) and H_4L = disalicylaldimine oxamide, di - (*o*-hydroxyacetophenoneimine)oxamide, disalicylaldimine succinamide or di-(*o*-hydroxyacetophenoneimine)succinamide, have been prepared and characterized by elemental analysis, IR and electronic spectroscopic studies and magnetic moment data[206]. The structures of most of the Cu(II) complexes and some of the Ni(II) and Co(II) complexes were planar whereas other Ni(II) complexes were distorted octahedral. Other Co(II) complexes were square pyramidal in geometry. Small magnetic moments of some of the complexes have been related to M-M interactions *via* oxo-bridge structures.

Solid complexes of Pb(II) with unsymmetrical Schiff-base ligands (H_2L) derived from the condensation of 2-aminobenzophenone, thiosemicarbazide and semicarbazide with salicylaldehyde, 2-hydroxynaphthaldehyde and *o*-hydroxyacetophenone have been synthesized by Singh[207]. The resultant Schiff base ligands and the complexes were characterized by elemental analysis, conductance measurements, molecular weight measurements and UV–Vis, FTIR, ^{1}H NMR, and ^{13}C NMR spectral techniques. The spectroscopic studies proposed that the ligands acted as dibasic tetra-dentate ONNO/ONNS donors. From the micro analytical data, the stoichiometries of the complexes were found to be 1:1 (metal:ligand).

A series of novel symmetric Schiff bases derived from 1,2-diaminoethane, salicylaldehyde (H_2L_1) and *o*-hydroxyacetophenone (H_2L_2) have been prepared and reported by El-Sonbati *et. al*[208]. They have isolated and characterized the ligands and metal complexes by elemental analyses, magnetic moment and UV-Visible and IR spectroscopic measurements. IR spectra showed that the ligands acted as dianionic- or neutral tetra-dentate donors. The anticipated geometry of the diamagnetic NiL_2 was 4-coordinate square planer. The electronic spectrum showed that the structure of $[Cu_2(H_2L_1)Cl_4(OH_2)_4]$ complex was distorted octahedral. The polarographic reduction of the Schiff bases was investigated in Britton-Robinson buffer solutions at p^H 3–12.

Syntheses of some new Mo(II) complexes with the composition, $MoO_2L.MeOH$, where LH_2 = Schiff base derived from salicylaldehyde, 2-hydroxy-1-naphthaldehyde, *o*-hydroxyacetophenone, *o*-hydroxybenzene, pyridoxal and thiosemicarbazide, S-methyldithiocarbazone or S-benzyldithiocarbazate were reported by Syamal *et. al*[209]. The complexes were characterized by elemental analysis, IR-, ^{1}H NMR- and electronic- spectroscopy, conductance, molecular weight and magnetic susceptibility measurements. The 6-coordinate complexes were monomers, nonelectrolytes and diamagnetic. The Schiff bases acted as dibasic tridentate ligands.

Novel Ru(II) complexes were reported by T. D. Thangadurai *et. al*[210]. The complexes, [Ru(CO)(B)(LL′)(PPh_3), where, LL′ = tridentate Schiff bases and B = PPh_3, pyridine, piperidine or morpholine have been synthesized by reacting [RuHCl(CO)(PPh_3)$_3$] or [RuHCl(CO)(PPh_3)$_2$(B)] with the Schiff bases containing O, N, and X donor atoms *viz.*, salicylaldehydethiosemicarbazone, salicylaldehydesemicarbazone, *o*-hydroxyacetophenonethiosemicarbazone (X = S) and *o*-hydroxyacetophenonesemicarbazone. The new complexes were characterised based on their elemental analysis and spectral (IR, ^{1}H- and ^{31}P-NMR.) data.

6-coordinated Ru(II) complexes of the type, [Ru(CO)(PPh_3)(Z)(L)], where Z = PPh_3, pyridine (py) or piperidine (pip) and L = anion of the Schiff base where reported by R. Karvembu *et. al*[211]. The tridentate Schiff bases were synthesized by condensing anthranilic acid with acetylacetone, salicylaldehyde, o-vanillin or o-hydroxyacetophenone. The complexes were characterised based on analytical and spectroscopic techniques. The article summarised that the complexes were found to be effective catalysts for oxidation of primary alcohols to aldehydes in the presence of *N*-methylmorpholine-*N*-oxide (NMO) as co-oxidant. The Schiff bases and their Ru(II) complexes showed growth inhibitory action against pathogenic fungi, *Aspergillus flavus, Fusarium oxysporium* and *Rhizoctonia solan*.

Interesting mixed ligand complexes of Mn(II), Co(II), Ni(II), Cu(II), Zn(II), and Cd(II) were reported by H. M. Parekh *et. al.*[212] The biologically active Schiff bases, *ie*. Potassium salts of o-hydroxyacetophenoneglycine and bis-(benzylidene) ethylenediamine or thiophene-o-carboxaldene-p-toluidine were used as ligands. These complexes have been characterized on the basis of their elemental analysis, thermogravimetric analysis, magnetic measurements, and electronic- and infrared spectra. The complexes were found to have better antifungal activities as compared to the free ligands and metal salts but modest activities as compared to the standard fungicides.

Interesting MoO(III) and MoO_2(II) complexes have been synthesized with novel tri- and tetradentate Schiff bases derived by the condensation of salicylaldehyde, thiosalicylaldehyde, *o*-hydroxyacetophenone, 3-carboxysalicyclaldehyde or acetylacetone with aminoalcohols, polymethylenediamines and *o*-phenylenediamines and was reported by Dey *et.al*[213]. Mononuclear oxothiolato Schiff base complexes of Mo(V) have been prepared for the first time. Quadridentate Schiff bases derived from salicylaldehyde and substituted salicylaldehydes and o-phenylenediamine have also been successfully employed as ligand to isolate MoO_2(II) complexes in the solid state. Similar to other MoO_2(II) complexes of salicylaldehyde polymethylenediamine Schiff base ligands, the two oxygen atoms of the MoO_2 group were found to be *cis*- to each other. The probable structures of the ligands and complexes were assigned based on their elemental analyses, magnetic susceptibilities, molar conductances, IR, electronic and ^{1}H NMR spectral data.

C. SCOPE OF THE PRESENT INVESTIGATION

Schiff bases ligands and their transition metal complexes are always interesting areas of research in inorganic chemistry. The most mesmerizing features of these compounds are different modes of bonding, diverse structures and their fascinating applications. These compounds have potential applications as antimicrobial- and anticancer agents.

The significances of Schiff bases and complexes in bioinorganic chemistry, biomedical field, supramolecular chemistry, catalysis and material science, separation and encapsulation processes have been effectively reviewed this chapter. The review indicates that Schiff bases of diamine are not extensively studied as compared to those of mono amines. The diverse donor characteristics of such Schiff bases and various applications of such ligands and their complexes prompted us to undertake this investigation. Therefore, in the present investigation we have synthesized and characterized six novel Schiff bases derived from 1,2-ethylenediamines with two carbonyl compounds, acetoacetanilide, ethyl/methyl acetoacetate, o-vaniline and o-hydroxyacetopheneone. Further, their ligational behaviors have been assessed and several metal complexes have been synthesized and characterized. When transition metal salts and the ligand react in 1:1 molar ratio, there may be a chance of anion coordination as well. These ligands are expected to act as excellent chelating agents due to the presence of two azomethine groups and can function in bidentate or dianionic tetradentate manner.

6 novel Schiff base ligands considering in this investigations are given below.

1. **Acetoacetanilide-(1,2-ethylenediimine)ethylacetoacetate**
2. **Acetoacetanilide-(1,2-ethylenediimine)methylacetoacetate**
3. ***o*-Vanilin-(1,2-ethylenediimine)acetoacetanilide**
4. ***o*-Hydroxyacetophenone-(1,2-ethylenediimine)acetoacetanilide**
5. ***o*-Hydroxyacetopheneone-(1,2-ethylenediamine)ethylacetoacetate**
6. ***o*-Vanilin-(1,2-ethylenediimine)*o*-hydroxyacetophenone**

Complexes of VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) with these ligands have been prepared and characterized. The acetate, chlorides or sulphate salts of these transition metals were used for complex preparation. In order to explain the properties and structures of the ligands and their metal complexes, elemental analysis, conductance –and magnetic susceptibility measurements and electronic-, IR- and ^{1}H NMR spectral techniques were used. The thermal decomposition behaviors of some of the complexes have also been studied.

Antimicrobial properties, particularly antibacterial and antifungal actions of the two ligands and their selected complexes were studied. These results suggested that the metal complexes were better antimicrobial agents than the free ligands. Cytotoxic activities and antitumor behaviors of one of the ligand and its selected metal complexes were thoroughly investigated. The *in vitro* cytotoxic and antitumor studies of the copper complex suggested its use as a potential anticancer agent.

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Chapter II

REAGENTS, APPARATUS AND EXPERIMENTAL PROCEDURES

A brief description of the common reagents used, experimental details and procedures adopted for the synthesis, analysis and characterization of the ligands and their metal complexes are given in the following pages. The different types of instruments with their operational characteristics and references and materials used for the physico-chemical studies of the ligands and complexes are also given. However, all specific synthetic procedures and experimental set up are explained in the appropriate chapters.

A. METAL SALTS

The metal salts used in this study were BDH AnalaR quality. Mainly chlorides, sulphates, nitrates or acetate of VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) were used for the synthesis of Schiff base complexes.

B. SOLVENTS

The solvents used for the synthesis, extraction and recrystalization of the ligands and the complexes were ethanol, methanol, DMF, DMSO, petroleum ether, etc. Commercially available solvents, like ethanol and methanol were purified by standard methods[1-3]. Others were E. Merck reagent grade and were used as such. The solvents, such as methanol and dimethyl formamide used for spectral and conductivity measurements were of spectroscopic grade.

C. LIGANDS

The ligands were synthesized from ethylacetoacetate, methylacetoacetate, acetoacetanilide, *o*-vanilin, *o*-hydroxyacetophenone and 1,2-ethylenediamine. They were prepared as follows:

1. Preparation

For the preparation of the ligands 1 and 2, ethyl/methylacetoacetate and acetoacetanilide in minimum amount of methanol was added to 1,2-ethylenediamine in methanol in a 250 ml round bottom flask in 1:1:1 molar ratio. Added a few drops of mineral acid as dehydrating agent. The mixture was allowed to reflux for 2 h. After the completion of the reaction, the mixture was slowly cooled in ice bath when off-white crystals seperated. The product was filtered and washed with ethanol and dried over anhydrous calcium chloride.

For the preparation of ligands 3 and 4 we have chosen *o*-vanilline and *o*-hydroxyacetophenone respectively, instead of ethy/methylacetoacetate in the procedure described above. Ligand 5 was synthesized by reacting *o*-hydroxyacetophenone and ethylacetoacetate with 1,2-ethylenediamine. For the preparation of the ligand 6, *o*-vanillin and *o*-hydroxyacetophenone were used as two carbonyl compounds.

Six novel Schiff base ligands synthesized in the present work are given below,

1. Acetoacetanilide-(1,2-ethylenediimine)ethylacetoacetate
2. Acetoacetanilide-(1,2-ethylenediimine)methylacetoacetate
3. *o*-Vanilin-(1,2-ethylenediimine)acetoacetanilide
4. *o*-Hydroxyacetophenone-(1,2-ethylenediimine)acetoacetanilide
5. *o*-Hydroxyacetopheneone-(1,2-ethylenediamine)ethylacetoacetate
6. *o*-Vanilin-(1,2-ethylenediimine)*o*-hydroxyacetophenone

D. COMPLEXES

Ethanolic solutions of the salts of VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) or Hg(II) was added to an DMSO/DMF solution of the ligand and the mixture was refluxed for 4 h. It was then cooled and allowed to evaporate. The solid complexes formed were filtered off, washed several times with petroleum benzene and finally with methanol. They were dried over anhydrous calcium chloride.

E. ANALYTICAL METHODS

Semimicro analyses were carried out by standard methods to check the purity of the compounds. Known methods were used for the estimation of the percentage amount of metals in the complexes[4]. For the estimation of metal and sulphur, a known amount of the complex was digested with a mixture of concentrated nitric acid (10 ml) and 2 or 3 drops perchloric acid. The digestion process was repeated for 3 or 4 times by adding fresh amount concentrated nitric acid. Finally, the process was carried out with concentrated hydrochloric acid. The digested mass was extracted with distilled water and used for the estimations. Copper present in the solution was estimated iodometrically using standard sodium thiosulphate solution. Zinc was determined by EDTA titrimetric method. Iron, nickel and sulfur were estimated gravimetrically. Iron was precipitated as ferric hydroxide in ammoniacal medium, ignited and weighed as Fe_2O_3. Chlorine was estimated argentometric using $AgNO_3$.

1. Elemental analysis

The percentage of carbon, hydrogen and nitrogen present in the ligands and the complexes were found out from elemental analysis. The elemental analysis was carried out by making use of the instrument, VarioEL III CHN analyzer at STIC CUSAT Cochin

F. PHYSICO-CHEMICAL MEASUREMENTS

The physico-chemical analysis of the ligands and complexes were accomplished using molar conductance measurement, magnetic susceptibility measurements, TG analysis and IR, ^{1}H-NMR and electronic spectral studies.

1. Molar conductance measurements

The determination of conductance data of coordination compounds and the use of such data follows structural elucidation back to the commencement of serious studies in the field of coordination chemistry. Thus Werner and Miolati[5] were able to use conductance data in aqueous solution in some of their earliest work on ammines. However, except for the simplest complexes of inorganic ligands, the use water as a solvent for conductance purpose is often undesirable because of the problems of hydrolysis or is impracticable because of lack of solubility. Accordingly, the use of water for such studies has declined and the use of organic solvents has increased rapidly, particularly over the last twenty years. Unfortunately, for a number of such solvents which have been used for the studies of coordination compounds, different ranges of conductance are reported for a particular electrolyte type. The wide variations in the type of complexes studied and the difference in experimental conditions used, have contributed much confusion in the use of molar conductance values in the structural elucidation of coordination compounds. Even for the commonly used solvents such as acetone, a cursory examination of the literature reveals conflicting ranges of conductance data, incorrect assignment of electrolyte type, and unjustified correlations with possible structures[6,7].

The electrical conductance measurements of the complexes were carried out by Systronic Conductivity Bridge, model 305 and dip type cell (cell constant = 1.083) calibrated with a 1 Molar aqueous solution of A. R potassium chloride. Corrections were applied on the basis,

$$\mathbf{L_{SOLUTION} = L_{SOLUTE} + L_{SOLVENT}}$$

where, L is the respective specific conductance in dimethylsulphoxide solution of the complex and have the concentration about 10^{-3}M.

2. Magnetic measurement

The magnetic susceptibility measurements of the complexes were carried out by Gouy method at room temperature using a Sherwood Scientific magnetic susceptibility balance and $Hg[Co(NCS)_4]$ as the calibrant. The diamagnetic corrections, using Pascal's constants, were applied by adding the diamagnetic contributions of various atoms and structural units. The effective magnetic moments were calculated from the corrected molar susceptibilities.

3. Electronic spectra

Electronic spectroscopy (UV-Vis spectroscopy) is the study of electronic transitions of a chemical compounds from its ground to excited state energy level by the absorption of electromagnetic radiation (mainly ultraviolet and visible region). The study of electronic absorption spectroscopy gives important information about the magnitude of energy gaps between the ground- and the excited electronic energy states of the metal ion, color of the complex, the extend of covalency in metal-ligand bonds, the position of metals and the ligands in the spectrochemical series and nephelauxetic series, etc,.

UV-Vis spectra of the soluble complexes were recorded using their solutions (10^{-3} M) in ethanol or methanol on a Jasco UV-Visible spectrophotometer model V-550. In the case of insoluble or partially soluble complexes, the spectra were recorded using a mull technique (solid state).[8]

4. IR spectra

When infrared rays are passed through a sample of organic compounds or metal complexes, some of the frequencies are absorbed, while other frequencies are transmitted through the sample. If we plot absorbance or transmittance against frequency, the result is an Infrared spectrum. Infrared spectroscopy is, therefore, basically vibrational spectroscopy. Different bonds have different vibrational frequencies, and we can detect the presence of a bond in a molecule by identifying its characteristic frequency as an absorption band in the infrared spectrum.

The infrared spectra of the ligands and the complexes, in the range 4000-400 cm^{-1} were recorded using KBr pellets on a Jasco FTIR 4100 spectrometer.

5. ^{1}H-NMR spectra

The ^{1}H- NMR spectra of ligands were recorded in $CDCl_3$ or DMSO-d_6 on a Bruker Avance-III, 400MHz instrument at STIC cusat Cochin.

6. Thermal analysis

Thermogravimetric Analysis (TG) determines the weight changes of a sample, as a function of temperature or time. The thermal decomposition studies of selected complexes in air carried out on a TG instrument, Perkin Elmer, Diamond model: STA 600 instrument at STIC CUSAT Cochin.

The experimental methods adopted and the procedures of antimicrobial- and anticancer studies are presented in PART-III, BIOTOXIC EVALUATION of the thesis.

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Chapter III

SYNTHESIS AND CHARECTERISATION OF SCHIFF BASE COMPLEXES DERIVED FROM ETHYLACETOACETATE AND ACETOACETANILIDE WITH 1, 2-ETHYLENEDIAMINE

In 1864, German scientist, Hugo Schiff synthesized a new group of organic compounds[1], imines, which are frequently referred to as Schiff bases. The preparative methods of these compounds are simple and elegant. They are prepared by the condensation reaction between carbonyl compounds and aromatic or aliphatic amines, in general by refluxing in alcohol. Schiff bases are often used as ligands in the area of coordination chemistry. The most common examples of these ligands are those derived from salicylaldehyde. They have been studied widely due to their easiness of preparation and their ability to bring changes both satirically and electronically.

The chemistry of Schiff bases is very diverse. They can coordinate in a monodentate[2] as well as polydentate[3] fashion to metal ions. Novel Schiff bases and their metal complexes have been studied as antibacterial agents[4-6], antifungal agents[7,8], antitumor drugs[9-11] and catalysts[12-18].

Even though the binding capacities of simple Schiff bases to metals have been widely studied, the interaction of those with two azomethine groups in a molecule have not been studied much. In Schiff base compounds, the imines nitrogen can act as an inter- or intra-molecular hydrogen bond acceptor. Hydrogen bonding interactions are significant because of their relevance in the biological systems. The nature and strength of such interactions between the molecules can influence the uptake of the medicine in the body.

Ethylacetoacetates or β-keto esters, especially simple and substituted one are usually known as good substrates for several ketoreductases (plant, microbial and recombinant, etc.,) for the asymmetric synthesis of the corresponding β-hydroxyesters. Five enantiopure β-hydroxyesters are useful precursors for the synthesis of various small organic molecules and are regarded as well explored chiral materials. Furthermore, β-keto esters form the basis for the manufacture of numerous natural products, pheromones and additives for paints. They are also of huge attention as chemical intermediates in the polymer and agriculture industries and extensively employed as flavour and fragrance in food and beverage industry[15]. Owing to their diverse applications, several synthetic procedures, which engage both homogeneous and heterogeneous catalysts, including strong acids, soluble base catalysts, metal salts, amine, zeolites, titanosilicates and enzymes, have been reported for the preparation of β-keto esters[16-22].

We are interested in the synthesis, structure and coordination chemistry of novel Schiff base ligands[23-32]. As a part of our ongoing studies on the structures and properties of polydentate Schiff base ligands, we report in this chapter the synthesis and characterization of a Schiff base derived from the condensation reaction of ethylacetoacetate and acetoacetanilide with 1,2-ethylenediamene and its complexes of VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II). The characterization was done based on elemental analysis, magnetic moment- and molar conductance measurements, IR, ^{1}H NMR and electronic spectral data.

A. EXPERIMENTAL

1. Materials and methods

For the preparation of the ligand-, ethylacetoacetate, acetoacetanilide and ethylenedaimene were used. The metal salts used in this study were BDH AnalaR quality. Mainly chlorides and sulphates of VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) were used for the synthesis of complexes.

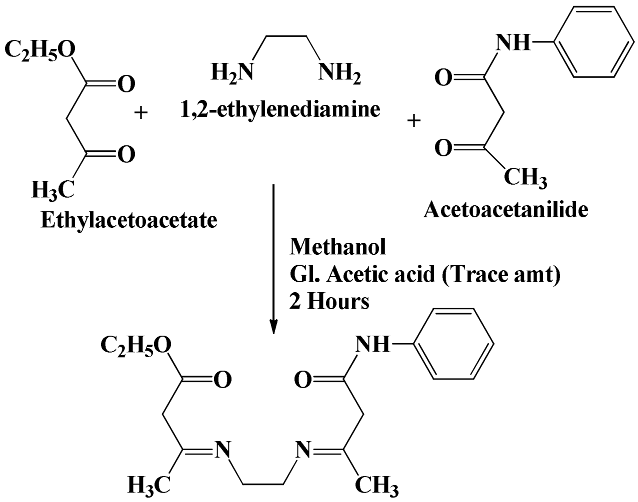
The solvents used for the synthesis, extraction and recrystalization of the ligand and the complexes were ethanol, methanol, chloroform, DMF, DMSO, petroleum benzene, diethyl ether, etc. Commercially available solvents, like ethanol and methanol were purified by standard methods[33]. Others were E. Merck reagents and were used as such. The solvents, such as methanol and dimethyl formamide used for spectral and conductivity measurements were of spectroscopic grade.

2. Synthesis

a. Acetoacetanilide-(1,2-ethylenediimine)ethylacetoacetate (AcEE)

A mixture of ethylacetoacetate (0.025 mol) and acetoacetanilide (0.025 mol) in minimum amount of methanol was added to 1,2-ethylenediamine (0.025 mol) in methanol in a 250 ml round bottom flask. Added a few drops of mineral acid as dehydrating agent. The mixture was allowed to reflux for 2 h. Completion of the reaction was confirmed by thin-layer chromatographic (TLC) studies on a pre-coated silica gel F_{254} plate from Merck. After the completion of the reaction, the mixture was cooled in an ice bath till the off-white crystals separated. The product was filtered, washed with ethanol and dried over anhydrous $CaCl_2$. **(Scheme. 1)**

Scheme.1 Scheme of the preparation of the ligand, Acetoacetanilide-(1,2-ethylenediimine)ethylacetoacetate (AcEE)



***The systematic IUPAC name of the compound is: (E)-ethyl-3-((2-((E)-(4-oxo-4-(phenylamino)butan-2-ylidene)amino)ethyl)imino)butanoate. But for the sake of convenience the name 'Acetoacetanilide-(1, 2-ethylenediimin)ethylacetoacetate' and the short form 'AcEE' are adopted in this thesis.**

b. Complexes

Methanolic solution of the metal salt (0.005 mol in 20 ml ethanol) was added to a solution of the ligand (0.005 mol in 20 ml DMSO) and the mixture was refluxed for about 4 h. It was then cooled and allowed to evaporate the solvent to reduce approximately half of the total volume. The solid complexes formed were filtered off, washed several times with petroleum benzene and finally with methanol and were dried over anhydrous calcium chloride. (**Table. 1**)

Table. 1: Physical properties of the complexes			
Si No	**Metal Salt Used**	**Color**	**Melting point**
1.	$VOSO_4.H_2O$	Greenish brown	289°C
2.	$CrCl_3.2H_2O$	Green	<300°C
3.	$MnSO_4.5H_2O$	Brown	<300°C
4.	$FeCl_3.6H_2O$	Dark red	298°C
5.	$CoCl_2.5H_2O$	Light red	275°C
6.	$NiCl_2.2H_2O$	Brown	265^0C
7.	$CuCl_2.2H_2O$	Blue	290^0C
8.	$ZnSO_4.7H_2O$	White	$<300^0C$
9.	$CdCl_2$	White	$<300^0C$
10.	$HgCl_2$	White	295^0C

B. RESULTS AND DISCUSSIONS

The data obtained from the analytical- and physico-chemical studies have been correlated to explain the properties, structures and bonding of the compounds.

1. Characterization of the ligand

The Schiff base ligand derived from ethylacetoacetate, acetoacetanilide and 1,2-ethylenediamine was off-white colored crystals, soluble in non-polar solvents like DMSO, benzene, etc. The homogeneity and purity of the ligand was tested by TLC technique. Melting point (180^0C) of the ligand was determined using a Fisher-Johns apparatus. The ligand was characterized by elemental analysis, IR- ^1H NMR- and UV-Vis spectral studies.

a. Elemental analysis

The ligand was subjected to elemental analysis on a CHN-instrument. The experimentally found and calculated percentages of C, H and N were in good agreement, confirming its molecular formula as, $C_{18}H_{25}N_3O_3$. **(Table. 2)**

Table. 2 Elemental analysis of the ligand, AcEE

Ligand	Carbon (%)		Hydrogen (%)		Nitrogen (%)	
	Found	Calculated	Found	Calculated	Found	Calculated
$C_{18}H_{25}N_3O_3$	64.01	65.23	6.99	7.66	13.00	12.68

b. ^{1}H NMR spectrum

The ^{1}H NMR spectrum of the ligand, AcEE was recorded in DMSO-d_6. The spectrum showed a number of peaks that were characteristic of the compound[34,35]. A sharp singlet at 9.23 ppm may be assigned to the -NH proton of acetoacetanilide moiety. The signals observed in the range 7.61-7.42 ppm may be assigned to the different types of aromatic protons of acetoacetanilide moiety. There were singlets at 3.34 and 3.36 ppm, which may be attributed to the active methylene protons of acetoacetanilide and ethylacetoacetate moieties, respectively. A quartet appeared at 4.13 ppm and a triplet at 1.29 ppm was, respectively, due to the -CH_2 and –CH_3 protons of the ethoxy group of ethylacetoacetate. The triplet appeared at 2.68 ppm may be assigned to the methylinic protons of diimine moiety of the ligand. The inductive effects of the nitrogen atoms might be responsible for the higher value. A singlet appeared at 1.91 ppm may be assigned to the protons of the –CH_3 groups on either sides of the imine group. (**Fig. 1 &Table. 3**)

Fig. 1, ^{1}H NMR spectrum of ligand, AcEE

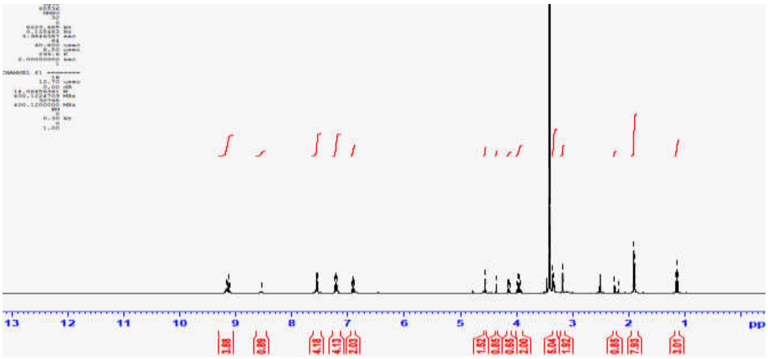


Table. 3, ^{1}H NMR data of ligand, AcEE		
Si.No	**Chemical shift (ppm)**	**Assignment**
1.	**9.23 (s)***	**-NH proton**
2.	**7.61-7.43 (m)**	**Aromatic protons**
3.	**3.34 (s)**	**-CH_2 active methylene proton of acetanilide**
4.	**3.36 (s)**	**-CH_2 active methylene proton**
5.	**4.13 (t)**	**-CH_3 proton of –OC_2H_5**
6.	**1.29 (q)**	**-CH_2 proton of –OC_2H_5**
7.	**2.68 (t)**	**two -CH_2 protons of imine group**
7.	**1.91 (s)**	**-CH_3 proton of either side of imine group**
***s= singlet, t= triplet, q= quartet**		

c. IR spectrum

The IR spectrum of the ligand, AcEE showed a number of absorption bands, which were characteristic of various functional groups present in it. Assignments were made on the basis of the spectra of the analogous compounds, known earlier[36,37]. The probable assignments are given in the **Table. 4**. The IR spectrum of the ligand showed a medium intensity band at 3100 cm^{-1} and a strong one at 1649 cm^{-1} characteristic stretching of –NH- and >C=O of amide group (-CO-NH-), respectively.

The bands present at 1617and 1244 cm^{-1} were assigned to the stretching vibration of –C=N and =N-C-, respectively. The band at 3063 cm^{-1} may be assigned to the aromatic –CH stretching and that at 2905 cm^{-1} to the –CH stretching of the methylene group. The bands at 2967 and 2939 cm^{-1} were due to the symmetric- and asymmetric stretching vibrations of CH_2 group. A sharp band at 1647 cm^{-1} may be due to $\upsilon_{C=O}$ of ethylacetoacetate moiety. The characteristic bands due to the stretching of –C=O in the acetoacetanilide and ethylacetoacetate, in the range, 1660-1668 cm^{-1} were not present in the spectrum of the ligand, which indicated the complete condensation of the carbonyl compounds and amine. A sharp band at 1210 cm^{-1} may be due to the υ_{C-O} of ethoxy group. **(Table. 4 & Fig. 2)**

Fig. 2: IR spectrum of the ligand, AcEE

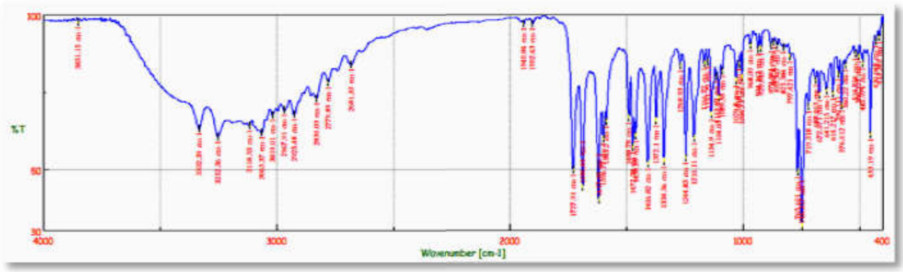
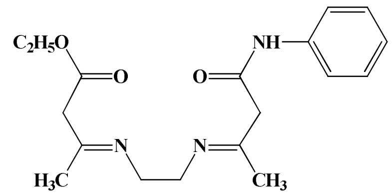


Table. 4. Significant IR bands of ligand, AcEE and their assignments	
Band frequency* (cm^{-1})	**Assignment**
3100 **1649**	**υ_{NH} amide** **$\upsilon_{C=O}$ amide**
1617	**$\upsilon_{>C=N}$ of ethylacetoacetate moeity**
1647	**$\upsilon_{>C=O}$ (keto)**
3063 **2905**	**υaromatic –CH** **υ_{-CH2} (Methylene)**
1244	**$\upsilon_{>C-N-}$**
1616 **1559**	**δ in plane –CH (aromatic)**
1210	**υ_{-CO-} (ethoxy)**
874 **819**	**δ out of plane –CH (aromatic)**

d. Electronic spectrum

The electronic spectrum of the ligand was recorded in DMSO at room temperature. The peak at 34714 cm^{-1} was attributed to $\pi \rightarrow \pi^*$ transition of aromatic part of the ligand. A peak at 23529 cm^{-1} was due to the $n \rightarrow \pi^*$ transition of the non-bonding electrons present on the oxygen of the keto (>C=O) groups and nitrogen of the azomethine (C=N) groups in the ligand[38]. From the above data, the following structure was assigned to AcEE (**Fig. 3**)

Fig. 3, Structure of the ligand, AcEE (LH_2)



2. Characterization of metal complexes

a. Analytical data

All the complexes were found to be colored [except those of Zn(II), Cd(II) and Hg(II)], non-hygroscopic and photo-stable. They were soluble in DMF and DMSO but only sparingly soluble in common organic solvents. The data obtained from analytical and molar conductance studies in DMF showed that the complexes have the formulae as shown in **Table. 5**. Aqua complexes were obtained for Cr(III), Mn(II), Co(II) and Ni(II). The magnetic- and various spectral data also confirmed the suggested molecular formulae. (**Table. 5**)

Table. 5. Analytical data of complexes

Empirical Formula	F*. Wt	Elemental %, Found (Calculated)				
		Metal	C	H	N	Anion
$(VO)C_{18}H_{23}N_3O_3$	396	12.01 (12.85)	53.99 (54.55)	5.06 (5.85)	9.96 (10.60)	
$CrC_{18}H_{25}N_3O_4Cl$	417	12.00 (12.46)	51.01 (51.79)	5.93 (6.52)	9.97 (10.07)	8.34 (7.83)
$MnC_{18}H_{27}N_3O_5$	420	12.01 (13.07)	52.00 (51.43)	7.00 (6.43)	10.99 (10.06)	----
$FeC_{18}H_{25}N_3O_3Cl_3$	495	10.96 (11.31)	48.00 (48.80)	6.00 (5.10)	7.99 (8.51)	20.89 (21.55)
$CoC_{18}H_{27}N_3O_5$	424	14.11 (13.99)	51.05 (50.09)	6.01 (6.30)	10.58 (9.90)	---
$NiC_{18}H_{27}N_3O_5$	423	14.01 (13.84)	51.00 (50.97)	6.05 (6.42)	10.01 (9.92)	---
$CuC_{18}H_{23}N_3O_3$	392	15.91 (16.07)	56.05 (55.10)	5.95 (5.86)	9.96 (10.71)	---
$ZnC_{18}H_{23}N_3O_3$	393	15.00 (16.16)	53.99 (54.76)	5.02 (5.87)	9.70 (10.64)	---
$CdC_{18}H_{23}N_3O_3$	441	2 5.01 (25.44)	48.00 (48.93)	6.00 (5.25)	8.01 (9.51)	---
$HgC_{18}H_{23}N_3O_3$	529.98	37.01 (37.85)	41.01 (40.79)	4.00 (4.37)	7.00 (7.93)	---

b. Molar conductance data

Molar conductance studies of electrolytic solutions have always been exciting for chemists. The studies of electrolytic behaviors of metal complex solutions provide brief insight of their natures and compositions. These studies provide a clue of the number of ions present in a particular solution responsible for the conduction of electric current and, thereby, quite significant structural information can be gathered. Molar conductance data are exploited to determine electrolytic and non-electrolytic character of the metal complexes. Besides, molar conductance data have been used to predict the geometries of metal complexes. In addition, molar conductance values have been used to establish metal-ligand stoichiometry. Finally, the structural changes of metal complexes in different solvents are discussed in terms of their molar conductance measurements[39].

The molar conductances at room temperature were determined using 10^{-3} M solutions of the complexes in DMSO and are given in the **Table. 6**. The molar conductance values in DMSO were in the range 11-55 $\Omega^{-1}mol^{-1}cm^2$, indicating the non-electrolytic nature of the complexes, accordingly, they were assigned formulae. Analytical data and spectral studies also supported the suggested formulae.

Table. 6. Molar conductance of complexes in DMSO

Si No:	Complexes	Λ_m ($\Omega^{-1}mol^{-1}cm^2$)
1.	[(VOL]	55
2.	[CrL(H_2O)Cl]	34
3.	[MnL(H_2O)$_2$]	27
4.	[Fe(L2H)Cl_3]	55
5.	[CoL(H_2O)$_2$]	34
6.	[NiL(H_2O)$_2$]	42
7.	[CuL]	34
8.	[ZnL]	11
9.	[CdL]	35
10.	[HgL]	25

L = $C_{18}H_{23}N_3O_3$

c. Magnetic moment data

Measurements of magnetic susceptibility constitute one of the most important experimental routes by which the chemists can easily and quickly acquire the information on the structure and bonding of transition metal complexes. It has been used to characterize a wide range of systems containing metals such as coordination complexes, metallic alloys and solid-state materials. The majority of the organic compounds and compounds of main group elements have all the electrons in paired state and therefore, they are diamagnetic molecules with very small magnetic moments. Most of the transition metal elements have at least one oxidation state with an incomplete d sub-shell. Magnetic measurements, mainly for the first row transition elements, give information about the number of unpaired electrons. The number of unpaired electrons provides information about the oxidation state and electron arrangement.

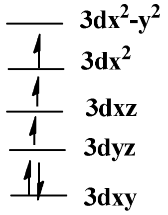
The ferromagnetic Cu(II) complexes are quite common, but the ferromagnetic oxovanadium(IV) complexes are rare[43]. Similarly, in an VO(II) complex with d^1 electron in the d_{xy} orbital, the ferromagnetic interaction is expected to be also weak[44]. VO(II) complex of the Schiff base derived from salicylaldehyde and ortho aminophenol exhibits a subnormal magnetic moment. The room temperature magnetic moments of such complexes lie in the range 0.77 – 1.55 B.M[40-42]. In the present case, the [VOL] complex exhibited a μ_{eff} value of 1.73 B.M. which is very close to the spin-only value for 1 unpaired d electron[45]. This indicates that the compound is monomeric and without any intermolecular association in solid state.

Cr(III) complexes, having d^3 electronic configuration are mostly the octahedral in geometry with $^3A_{2g}$ ground term. Due to low spin-orbit coupling, Cr(III) compounds are expected to exhibit magnetic moments values very close to the spin-only value of 3.7 B.M[46]. Slightly lower values are reported for polynuclear complexes due to the magnetic exchange between neighbouring chromium ions through the bridging ligands leading to anti-ferromagnetic coupling[46]. In the present investigation, AcEE Schiff base complex of Cr(III) showed a magnetic moment of 3.87 B.M. which indicated its octahedral geometry.

Both low-spin ($S = 1/2$) and high-spin ($S = 5/2$) Mn(II) complexes are known[47]. In both octahedral- and tetrahedral geometries, high-spin Mn(II) has a spin-only value of 5.91 B. M at room temperature. Magnetic moment values exhibited by octahedral low-spin Mn(II) complexes are close to 2.51 B.M. Experimental values of magnetic moments of high-spin octahedral Mn(II) complexes vary between 5.64 and 6.11 B.M. The magnetic moments of a number of Schiff base complexes of Mn(II) have been found to be significantly below the spin-only value. Their magnetic moment values range between 4.74 and 5.50 B.M at room temperature. These complexes may not be magnetically dilute and there are no obvious explanations for such low magnetic moment data. In the present case, the observed value was 5.72 B.M. indicating its octahedral geometry[47,48].

Fe(III) complexes are isoelectronic with Mn(II) complexes. Spin-only value of high-spin Fe(III) complex with d^5 configuration is 5.91 B.M, but for low-spin complex it is close to 2.52 B.M. Lower magnetic moment values observed in bridged binuclear species are due to appreciable anti-ferromagnetic coupling.

The Fe(III) complex showed μ_{eff} value of 3.96 B.M. It is comparable to the values reported earlier[68-70]. On the basis of the spin-only formula, this value of magnetic moment would correspond to three unpaired electrons (μ spin-only for 3 unpaired electrons is 3.87 B.M.). This, in turn, would point to a quartet state, ^4G, for the free ion. In the octahedral field this would split into 3 states ^4E, $^4T_2$ and $^4T_1$, the last mentioned being the lowest in energy. In the present case, the complex is expected to have square pyramidal geometry in the analogy with the other halogenated Fe(III) Schiff base complexes of known structure[68,69]. Hence, the $^4T_{1g}$ state splits into a singlet $^4A_2$ and a doublet ^4E under C_{4V} symmetry or into 3 singlets, $^4A_2$, $^4B_1$ and $^4B_2$ under C_{2V} symmetry. For such complexes, Martin and White suggested the following relative ordering of 3*d* orbitals; $3dxy < 3dxz = 3dyz < 3dx^2 < 3dx^2\text{-}y^2$. On this basis, they have assigned the following electronic configuration to the central cation. Such a configuration would leave the



dx^2-y^2 orbital free for dsp^3 hybridization leading to the square pyramidal geometry, as postulated by R. Dandel and A. Bucher[70].

Co(II) complexes with one unpaired electron may be either low-spin octahedral or planar but complexes with three unpaired electrons may be either tetrahedral or octahedral in geometries. Even though the spin-only value for 3 unpaired electrons is 3.89 B.M., the intrinsic orbital angular momentum in high-spin octahedral ground state ($^4T_{1g}$) of a Co(II) complex results in a considerable orbital contribution and leads to magnetic moment values between 4.7 and 5.2 B.M. at room temperature[50]. Tetrahedral high-spin Co(II) complex, with ground term ($^4A_2$) has no orbital contributions and the expected value of magnetic moment is 3.89 B.M. However, due to the mixing of the $^4T_2$ state by spin-orbit coupling, the moment values observed are in the range, 4.40-4.70 B.M. It has been reported that the magnetic moment values ranging from 2.5 to 2.9 B.M. are shown by low-spin square-planar Co(II) complexes[51,52]. In the present investigation, $[CoL(H_2O)_2]$ registered a magnetic moment value of 4.4 B.M. and therefore, it may be octahedral in geometry.

Tetrahedral Ni(II) complexes[53] exhibit high magnetic moment values in the range 3.62 to 4.01 B.M. which is due to substantial orbital contribution of the T ground state towards the spin-only value of 2.83 B.M., corresponding to the two unpaired electrons. Large distortions and inequalities in the fields of coordinated ligands are found to result in magnetic moments with small orbital contribution and the magnetic moment values are observed as low as 3.22 B.M.[54] Square-planar Ni(II) complexes have spin-singlet ground state and are diamagnetic. Five coordinated high-spin complexes are known to have magnetic moments in the range of 3.0 to 3.4 B.M [54]. Octahedral Ni(II) complexes ought to register magnetic moments almost equal to the spin-only value, as the ground state ‘A’ lacks orbital contribution. However, the observed magnetic moment values fall in the range, 2.60 to 3.30 B.M., due to spin-orbit coupling or higher state mixing with ground state[54]. In the present case, [$NiL(H_2O)_2$] registered a magnetic moment value of 3.32 B.M. indicating its octahedral geometry.

The complexes of Cu(II) generally have distorted octahedral geometry, but square planar or approximately tetrahedral geometries are also known for many complexes[55]. Stereochemistry has a little effect on the magnetic moments of Cu(II) complexes and values slightly higher than the spin-only value for one unpaired electron in d^9 electronic configuration are expected[55]. A regular octahedral Cu(II) complex has the ground term, ^2E_g and hence there is no orbital contribution. The spin-only magnetic moment value corresponding to one unpaired electron is 1.73 B.M., but the experimental values observed are usually in the range, 1.80 to 2.10 B.M[55]. The slightly higher value is due to the spin-orbit coupling[55]. The ground term in regular tetrahedral geometry being a triplet state ($^3T_2$), orbital contribution is to be expected and theoretically predicted value of μ_{eff} is 2.20 B.M[56]. But the observed values usually fall in the range, 1.95 to 2.00 B.M.[57] In the present case of AcEE Schiff base complex of Cu(II) registered a magnetic moment value of 2.01 B.M., indicating its tetrahedral geometry. **(Table. 7)**

Table. 7 Magnetic moment data of complexes

Si No:	Complexes	μ_{eff} (B.M)
1.	[(VOL]	1.73
2.	[$CrL(H_2O)Cl$]	3.87
3.	[$MnL(H_2O)_2$]	5.72
4.	[$Fe(L2H)Cl_3$]	3.96
5.	[$CoL(H_2O)_2$]	4.40
6.	[$NiL(H_2O)_2$]	3.32
7.	[CuL]	2.01

μ_{eff} = Effective magnetic moment, B.M = Bohr magneton

d. Electronic spectra

The study of electron absorption spectra, especially crystal field spectra of coordination complexes, provides important information such as magnitude of energy gaps between the ground- and the excited electronic energy states of the metal ions in the complexes, colors of the complexes, the extend of covalent character in metal-ligand bonds, the geometry of the complexes and the position of metals and the ligands in the spectrochemical- and nephelauxetic series, etc[58].

The 6- coordinate V(IV) exhibits one absorption band centered around 15,458 and 20,105 cm^{-1}, but in six coordinated VO(II) complexes, the situation is entirely different because of tetragonal compression. Even though three transitions are expected in such complexes, only two bands are seen. They are, one at 13,100 cm^{-1} due to $d_{xy} \rightarrow d_{xz}$, d_{yz} transition and other at 16,100 cm^{-1} due to the $d_{xy} \rightarrow d_{x^2-y^2}$ transition, the latter being a measure of 10 Dq. The 5- coordinate VO(II) complexes show three bands at 13,000, 17,000 and 25,600 cm^{-1}. These bands are assigned to the transitions, $^2B_2 \rightarrow {}^2E$ (ν_1), $^2B_2 \rightarrow {}^2B_1$ (ν_2), and $^2B_2 \rightarrow {}^2A_1$ (ν_3), respectively[59].

The electronic spectrum of [VOL] was recorded in DMSO at room temperature. It exhibited bands at 13,670, 19,598 and 24,300cm^{-1} which were assignable to transitions, $^2B_2 \rightarrow {}^2E$ (ν_1), $^2B \rightarrow_2$ $^2B_1$ (ν_2), and $^2B_2 \rightarrow {}^2A_1$ (ν_3), respectively, indicating its 5- coordinate mononuclear nature with distorted tetragonal pyramidal geometry[52]. It was consistent with the magnetic moment value of the complex.

The 6- coordinate Cr(III) belongs to the d^3 system and in an octahedral geometry three transitions are expected[59], which are

$$^4A_{2g} \rightarrow {}^4T_{1g}(P)$$
$$^4A_{2g} \rightarrow {}^4T_{2g}$$
$$^4A_{2g} \rightarrow {}^4T_{1g}(F)$$

The complex, hexaaqua chromium (III) chloride records three spin-allowed transitions at 17,405, 24,600 and 37,800 cm^{-1}. In the spectrum of the Cr(III) complex investigated here, two bands were observed at 17,150 and 22,450 cm^{-1} and were assigned, respectively, $^4A_{2g} \rightarrow {}^4T_{1g}$ and the $^4A_{2g} \rightarrow {}^4T_{2g}$ transitions characteristic of octahedral geometry. Octahedral environment of Cr(III) complex, exhibited a third transition corresponding $^4A_{2g} \rightarrow\ ^4T_{1g}$ (P) above 30000 cm $^{-1}$ but in this region the n→π* and π→π* intraligand bands are also observed.[60-62].

The hexa-coordinated high-spin Mn(II) belongs to the d^5 system. Tanabe-Sugano diagram corresponding to such a system exhibits only high-spin state. Russel-Saunders term is ^6S which in octahedral geometry is represented as $^6A_{1g}$. Since there is no excited state with the spin multiplicity of 6, all transitions in d^5 high-spin complexes are parity forbidden (spin forbidden and Laporte forbidden). Consequently, all electronic transitions have extremely low molar extinction coefficient values. Some electronic transitions of Mn(II) are,

$$^6A_{1g} \rightarrow\ ^4T_{1g}\ (P)$$

$$^6A_{1g} \rightarrow\ ^4E_g \text{ or } ^4A_{1g}$$

Usually the tales of CT bands overlap with these weak transitions, thus obscuring them. In the tetrahedral manganouse(II) complexes, the electronic transitions are still spin-forbidden but not parity forbidden, therefore, the electronic transitions are about hundred times stronger and the compounds have noticeable light yellow or pale green colour. They can also show yellow-green fluorescences. In the present case, electronic spectrum of the Mn(II) complex exhibited a number weak bands around 25,000 cm^{-1} which were assigned to d-d transitions of an octahedral complex. The light brown colour of $[MnL(H_2O)_2]$ and bands at 18,610, 22,900 and 24,900 cm^{-1} and were characteristic of octahedral geometry.

Some of the electronic transitions of 6- coordinate Fe(III) complexes are,

$$^6A_{1g} \rightarrow {}^4T_{1g}(G) \sim 18{,}621 \text{ cm}^{-1}$$

$$^6A_{1g} \rightarrow {}^4T_{2g}(G) \sim 23{,}255 \text{ cm}^{-1}$$

$$^6A_{1g} \rightarrow {}^4E_g(G) \sim 25{,}00 \text{ cm}^{-1}$$

$$^6A_{1g} \rightarrow {}^4A_{1g}(G) \sim 25{,}188 \text{ cm}^{-1}$$

Most of the electronic transitions of Fe(III) are at very high energy region and they give no information about the type of bands involving in charge-transfer. The whole interpretation and precise analysis become possible only by a full quantum mechanical analysis of the molecule. In the present investigation, [Fe(L2H)Cl_3] registered two bands, one at 25,400 $cm^{-1}$and a broad band at 19,607 cm^1 and registered a magnetic moment value of 3.96 B.M. These observation may be attributed to 5-coordinate square pyramidal geometry of the complex.

The 6- coordinate complexes of high-spin Co(II) are d^7 systems. In an octahedral geometry, the probable transitions are,

$$^4T_{1g} \rightarrow {}^4T_{2g} \quad \ldots\ldots \quad (\nu_1)$$
$$^4T_{1g} \rightarrow {}^4A_{2g} \quad \ldots\ldots \quad (\nu_2)$$
$$^4T_{1g} \rightarrow {}^4T_{1g}(P) \quad \ldots\ldots \quad (\nu_3)$$

In [$Co(H_2O)_6$]Cl_2, there are 3 spin- allowed electronic transitions, at 8,100 (ν_1), 16,000 (ν_2) and 19,400 cm^{-1} (ν_3). It has been found that in octahedral high-spin Co(II) complexes the ν_3 band, involving the one electron transition, is comparatively stronger than the ν_2 band involving two electron transition. The configurations of $^4T_{1g}$(F), $^4A_{2g}$(F) and $^4T_{1g}$(P) levels are $t_{2g}^5e_{2g}^2$, $t_{2g}^3e_{2g}^4$ and $t_{2g}^4e_{2g}^3$, respectively[63]. The ν_2 band, therefore, usually appears as a shoulder or often does not appear at all. The 4- coordinate tetrahedral Co(II) has a ground state term, ^4F which splits into the $^4A_{2g}$, $^4T_2$, and $^4T_1$(F) states. Besides, the excited term, ^4P changes to $^4T_1$(P). We expect three transitions which are,

$^4A_2 \rightarrow {}^4T_2$ (ν_1) (F),
$^4A_2 \rightarrow {}^4T_1$ (ν_2) (F) and
$^4A_2 \rightarrow {}^4T_1$ (P) (ν_3)[64]

In the present investigation, the spectrum of Co(II) AcEE complex showed three intense transitions with bands at 8,968, 14,925 and 24,390 cm^{-1}. They were assigned, respectively to the $^4T_{1g} \rightarrow {}^4T_{2g}$ (ν_1), $^4T_{1g} \rightarrow {}^4A_{2g}$ (ν_1) and $^4T_{1g} \rightarrow {}^4T_{1g}$ (P) (ν_1) transitions of a typical octahedral Co(II) complex[64].

The 6- coordinated Ni(II) complexes belong to d^8 system. We find that there are three spin allowed transitions, namely,

$^3A_{2g} \rightarrow {}^3T_{2g}$ (F) (ν_1)

$^3A_{2g} \rightarrow {}^3T_{1g}$ (F) (ν_1)

$^3A_{2g} \rightarrow {}^3T_{1g}$ (P) (ν_1)

The complex $[Ni(dipyridyl)_3]SO_4$ showed three electronic transitions at 12,650 (ν_1), 19,205 (ν_2), and 26,000 cm^{-1}. The last band cannot be considered as ν_3 because it has high molar extinction coefficient. It is rightly designated as a charge-transfer band. The complex, $(Et_4N)_2[NiCl_4]$ has two absorption bands at 7,549 and 14,250 cm^{-1}. For tetrahedral Ni(II) complexes, the expected transitions are, $^3T_1 \rightarrow {}^3T_2$ (ν_1), $^3T_1 \rightarrow {}^3A_2$ (ν_2) and $^3T_1 \rightarrow {}^3T_1$ (P) (ν_3). The square-planar Ni(II) complexes are generally yellow, red or brown in color. This may due to the presence of absorption bands of medium intensities in the range, 16,660 to 22,220 cm^{-1}. However, other colours are due to charge-transfer bands. The Ni(II) complex, investigated here showed transitions corresponding to octahedral geometry. Bands were identified at 8,650, 13,774 and 24,390 cm^{-1} and were assigned, respectively, to the following transitions;

$^3A_{2g} \rightarrow {}^3T_{2g}$ (F),

$^3A_{2g} \rightarrow {}^3T_{1g}$(F) ,

$^3A_{2g} \rightarrow {}^3T_{1g}$ (P)

The ratio of wave numbers of the transitions assigned as $^3A_{2g} \rightarrow {}^3T_{2g}$ (F) and $^3A_{2g} \rightarrow {}^3T_{1g}$(F) was found to be 1.6 confirming its octahedral geometry.

The 6- coordinate Cu(II) belongs to the d^9 system. We except a single absorption band representing the transition, $^2E_g \rightarrow {}^2T_{2g}$, ie 10Dq. The complex, $[Cu(H_2O)_6]Cl_2$ has a pale blue color and shows a broad band with two maxima at 9,400 and 12,600 cm^{-1}. The mean value of these two maxima, ie., 11,000 cm^{-1}, is taken as 10 Dq. This d^9 system is very sensitive to the Jhan-Teller distortion. In the present investigation, the spectrum of Cu(II) AcEE complex showed an intense transition at 13,510 cm^{-1} and was assigned to the $^2T_2 \rightarrow {}^2E$ [64] transition which indicated its tetrahedral geometry. (**Table. 8**)

Table. 8. Electronic spectra of complexes

Si. No:	Complexes	Bands (cm^{-1})	Assignments	Geometry
1.	**[(VOL]**	**13,670**	$^2B_2 \rightarrow {}^2E$	**Tetragonal Pyramid**
		19598	$^2B_2 \rightarrow {}^2B_1$	
		24300	$^2B_2 \rightarrow {}^2A_1$	
2.	**[CrL(H_2O)Cl]**	**17,150**	$^4A_{2g} \rightarrow {}^4T_1$ (P)	**Octahedral**
		22,450	$^4A_{2g} \rightarrow {}^4T_{2g}$	
3.	**[MnL(H_2O)$_2$]**	**18,610**	$^6A_{1g} \rightarrow {}^4T_{1g}$	**Octahedral**
		22,900	$^6A_{1g} \rightarrow {}^4T_{2g}$	
		24,900	$^6A_{1g} \rightarrow {}^4E_g$	
4.	**[Fe(L2H)Cl_3]**	**19,407**	$^6A_{1g} \rightarrow {}^4T_{2g}$	**Square pyramidal**
		25,400	**CT**	
5.	**[CoL(H_2O)$_2$]**	**8,968**	$^4T_{1g} \rightarrow {}^4T_{2g}$	**Octahedral**
		14,925	$^4T_{1g} \rightarrow {}^4A_{2g}$	
		24,390	$^4T_{1g} \rightarrow {}^4T_{1g}$ (P)	
6.	**[NiL(H_2O)$_2$]**	**8,650**	$^3A_{2g} \rightarrow {}^3T_{2g}$	**Octahedral**
		13,774	$^3A_{2g} \rightarrow {}^3T_{1g}$	
		24,390	$^3A_{2g} \rightarrow {}^3T_{1g}$	
7.	**[CuL]**	**13,510b**	$^2T_2 \rightarrow {}^2E$	**Tetrahedral**

e. IR spectra

The IR spectra of the complexes showed a number of absorption bands, which were characteristic of various functional groups present in it. Assignments (**Table. 9)** are given on the basis of analogous structures known earlier[36,37]. The IR spectrum of the ligand showed a medium intensity band at 3100 and a strong one at 1649 cm^{-1}, respectively, due to **ν** –NH- and **ν** –C=O of amide group (-CO-NH-). The band at 1649 cm^{-1} was absent in the spectra of all the complexes except that of [Fe(L2H)Cl_3]. This indicated that the –NH-CO-CH_2- (amide group) of acetoacetanilide moiety has undergone enolisation to –CH=C-OH and after deprotonation coordinated to the metal in these complexes. This was supported by the appearance of new bands around 1124 cm^{-1}, due to ν-c-o in the spectra of these complexes.

The band of medium intensity at 1617 cm^{-1} in the spectrum of ligand may be assigned to $\mathbf{\nu_{C=N}}$. However, in the spectra of all the complexes, this band was found to be shifted to a lower frequency region by a few cm^{-1} indicating the participation of azomethine nitrogens in coordination.

Disappearance of $\mathbf{\nu_{>C=O}}$ peak (1647 cm^{-1}) in the spectra of all the complexes, except that of Fe(III) complex (Figure 4a, Appendix I), indicated that the chelation took place through the deprotonated enolic oxygen (ethylacetoacetate moiety). In the spectra of the all complexes, except that of $[Fe(L2H)Cl_3]$ new stretching band were observed in the range, 1124 -1110 cm^{-1}, indicating the enolization of $–CH_2-C=O$ to $–CH=C-OH$ and subsequent coordination through the deprotonated oxygen of ethylacetoacetate part. From the above observations, it can be assumed that the ligand, AcEE coordinated with Fe in $[Fe(L2H)Cl_3]$ complex in a neutral bidentate mode without enolisation.

The band at 3063 cm^{-1} may be assigned to the aromatic –CH stretching and that at 2905 cm^{-1} to the –CH stretching of the methylene group. Sharp bands at the range 1210-1050 cm^{-1} were due to the $\mathbf{\nu_{C-O}}$ of ethoxy group.

A characteristic sharp band in the spectrum of VO(II) complex at 955 cm^{-1} has been assigned to non- ligand stretching of $\mathbf{\nu_{(V=O)}}$[52]. Broad bands ~ 3500-3415 cm^{-1} in the spectra of the complexes of Cr(III), Mn(II) and Ni(III) were attributed to the hydroxyl stretching modes of water molecules. In addition, strong bands ~ 864-973 and ~ 660 cm^{-1} suggested that the water molecules were coordinated.[65] Medium bands around 530 and 450 cm^{-1} in the spectra of all the complexes may be assigned[66] to $\mathbf{\nu_{(M-N)}}$ and $\mathbf{\nu_{(M-O)}}$, respectively. Bands at 410 cm^{-1} and 415 cm^{-1} in the spectra of Cr(III) and Fe(III) complexes indicated the presence of M-Cl bonds in these complexes. (**Table. 9& Fig. 4-7**)

Table. 9. Significant bands in the IR spectra of AcEE and its metal complexes

Compounds	Assignments and band frequencies (cm^{-1})							
	$\nu_{\text{-C=O}}$	$\nu_{\text{-C=N}}$	ν-amide	$\nu_{\text{-OH}}$ (H_2O)	$\nu_{\text{=C-O-}}$ (enolised)	$\nu_{\text{-M-N}}$	$\nu_{\text{-M-O}}$	$\nu_{\text{-M-Cl}}$
AcEE (LH_2)	1647	1617	3100 1649	---	----	-----	---	----
[(VOL]	1124	1605	3101 ---	----	1119, 1033	495	444	----
[$CrL(H_2O)Cl$]	1120	1610	3103 ---	3441	1119, 1033	517	445	410
[$MnL(H_2O)_2$]	1110	1608	3100 ---	3307	1112, 1045	505	440	---
[$Fe(L2H)Cl_3$]	1640	1606	3102, 1649	---	----	510	---	415
[$CoL(H_2O)_2$]	1123	1605	3102 ----	3456	1122, 1056	579	470	----
[$NiL(H_2O)_2$]	1120	1610	3100 ----	3347	1139, 1098	570	465	---
[CuL]	1112	1610	3103 ----	----	1114, 1106	528	478	----
[ZnL]	1118	1606	3102 ----	----	1115, 1041	538	473	----
[CdL]	1124	1609	3100 ----	----	1154, 1004	526	468	---
[HgL]	1122	1604	3103 ----	----	1149, 1046	516	455	---

Fig. 4: IR spectrum of Cr(III) complex

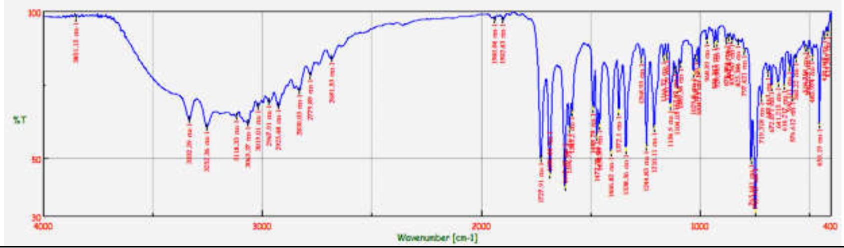


Fig. 5: IR spectrum of Co(II) complex

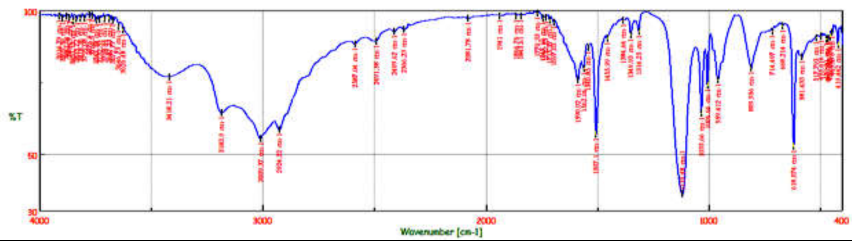


Fig. 6: IR spectrum of Ni(II) complex

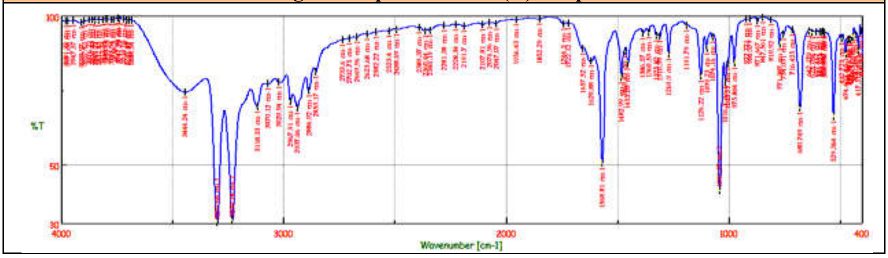
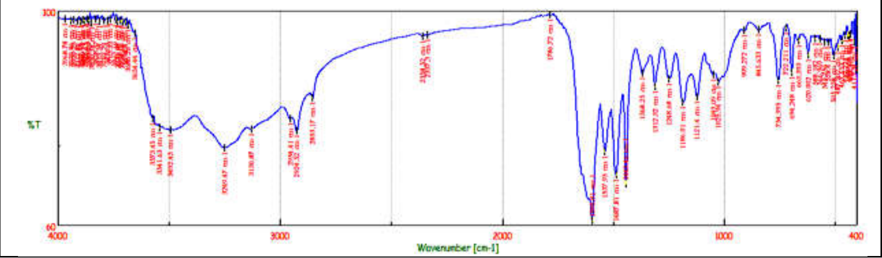


Fig. 7: IR spectrum of Cu(II) complex

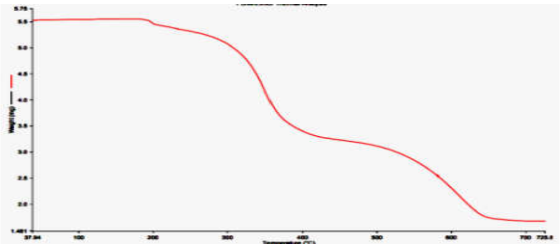


f. Thermal analysis

The thermal decomposition behaviors of the Co(II), Ni(II) and Cu(II) metal complexes were studied in air by heating from ambient temperature to 725°C. The TG curves of the Co(II) and Ni(II) complexes exhibited mass loss at the range 150-200°C, indicating the presence of the coordinated water molecule in them. (**Table. 10**)

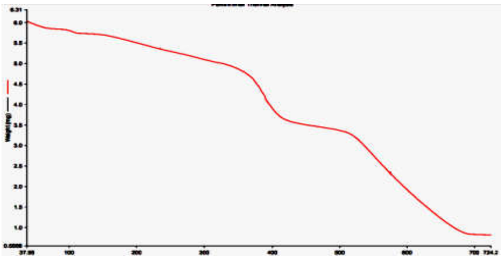
On the TG curve of Co(II) complex, The first stage of decomposition of Co(II) complex occurred in a temperature range from 200-250 ^{0}C, with a mass loss 7.2 % (theoretical 8.5 %). It may be attributed to the removal of two coordinated water molecule. The second stage, from 350 to 400 °C, with mass loss 37.2 % (theoretical 36. 5 %), corresponded to the decomposition of the coordinated part of the ligand, $C_6H_9NO_2$. The final stage, from 600 to 650 °C, with mass loss 75 % (theoretical 75%), corresponded to the decomposition of the remaining part of the ligand $C_{12}H_{14}N_2O$. The mass of the final residue corresponded to the stable cobalt oxide, CoO. (**Fig. 8**)

Fig. 8: TG thermogram of Co(II) complexes



The thermogram of the Ni(II) complex showed a mass loss of 9.0 % (theoretical 8.9 %) in the temperature range 100-150 °C indicating the loss of two coordinated water molecules. The anhydrous complex then showed a second decomposition in the range, 350-450°C, with a 38% (theoretical 37 %) mass loss, which may be attributed to the removal of the $C_6H_9NO_2$ from the ligand. The third stage, from 600 to 700 °C with mass loss 79% (theoretical 81%), corresponded to the decomposition of the remaining part of the ligand, $C_{12}H_{14}N_2O$. The mass of the final residue corresponded to the stable metal oxide, NiO. (**Fig. 9**)

Fig. 9: TG thermogram of Ni(II) complexes



The TG curve of the Cu(II) complex showed a two-stage decomposition pattern. The complex did not show any mass-loss in this range 150-200 ^{0}C and was stable up to 350 ^{0}C. This was due to the absence of coordinated water molecules in it. The first stage started from 350 to 400 °C with a mass loss of 29.1 % (theoretical 30.1%). This may be due to the decomposition of a part of the ligand, $C_6H_9NO_2$. The next stage, from 650-700°C with a mass loss of 77% (theoretical 76%), corresponded to the loss of the remaining coordinated part of the ligand, $C_{12}H_{14}N_2O$. The mass of the final residue correspond to the copper oxide, CuO. (**Fig. 10**)

Fig. 10: TG thermogram of Cu(II) complexes

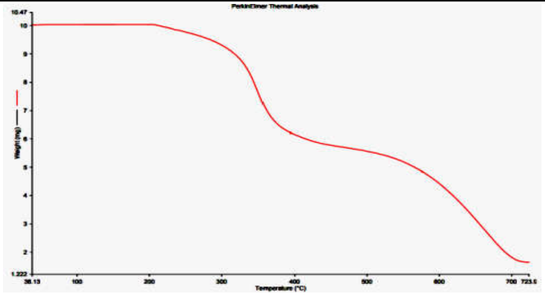


Table. 10: TG data of complexes

Complex	Stage	Temp range in TG (^{0}C)	Loss of mass in %		Assignment
			TG	Theoretical	
$CoL_1(H_2O)_2$	I Stage	200-250	7.2	8.5	Loss of two H_2O
	II Stage	350-400	37.2	36.5	Loss of $C_6H_9NO_2$
	III Stage	600-650	75	79.4	Loss of $C_{12}H_{14}N_2O$ and conversion to CoO
$NiL(H_2O)_2$	I Stage	100-150	9	8.9	Loss of two H_2O
	II Stage	350-450	38	37	Loss of $C_6H_9NO_2$
	III Stage	500-600	79	81	Loss of $C_{12}H_{14}N_2O$ and conversion to NiO
CuL	I Stage	350-400	29.1	30.1	Loss of $C_6H_9NO_2$
	II Stage	650-700	77	76	Loss of $C_{12}H_{14}N_2O$ and conversion to CuO

On the basis of above observations, the probable structures of the AcEE and its metal complexes of VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) are shown below: (**Fig. 11-17**)

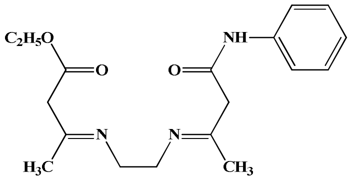
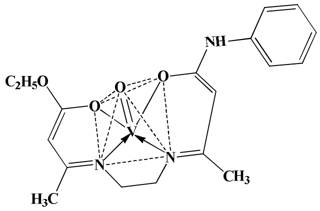
Fig. 11: Ligand, AcEE (L2H)	**Fig. 12: Structure of [VOL]**
	

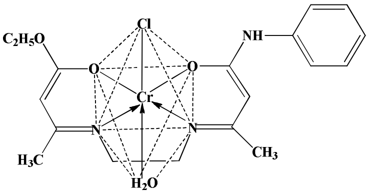
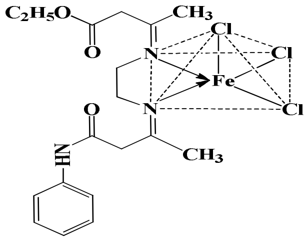
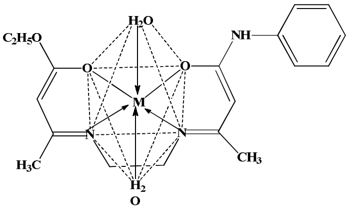
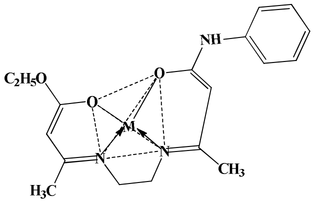
Fig. 13: Structure of [CrL(H_2O)Cl]	**Fig. 14: Structure of [Fe(L2H)(Cl_3)]**
	

Fig. 16: Structure of [ML(H_2O)$_2$], where M = Mn(II), Co(II) and Ni(II)	**Fig. 17: Structure of [ML], where M= Cu(II), Zn(II), Cd(II) and Hg(II)**
	

C. CONCLUSIONS

Coordination complexes of VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) with a multidentate ONNO donor Schiff base ligand, acetoacetanilide-(1,2-ethylenediimine)ethylacetoacetate (L2H) have been prepared and their physico-chemical properties have been studied. The ligand, acetoacetanilide-(1,2-ethylenediimine)ethylacetoacetate (L2H) was synthesized by condensation reaction of acetoacetanilide and ethylacetoacetate with 1,2-ethylenediamine in 1:1:1 molar ratio. The complexes have the general formulae, [(VOL], [CrL(H_2O)Cl], [MnL(H_2O)$_2$], [Fe(L2H)Cl_3], [CoL(H_2O)$_2$], [NiL(H_2O)$_2$], [CuL], [ZnL], [CdL] and [HgL]. Based on the analytical, magnetic and various spectral studies, geometries have been assigned to these complexes. [(VOL] complex was found to be tetragonal pyramidal, [CrL(H_2O)Cl], [MnL(H_2O)$_2$], [CoL(H_2O)$_2$] and [NiL(H_2O)$_2$] complexes were found to be octahedral, [Fe(L2H)Cl_3] was found to be square bypyramidal and [CuL], [ZnL], [CdL] and [HgL] complexes were tetrahedral.

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Chapter IV

SYNTHESIS AND CHARECTERISATION OF SCHIFF BASE COMPLEXES DERIVED FROM METHYLACETOACETATE AND ACETOACETANILIDE WITH 1, 2-ETHYLENEDIAMINE

Tetradentate Schiff bases coordinate with many metal ions forming the stable compounds[1,2]. Schiff bases with O and N donor atoms are good catalysts for various organic transformations[3-12]. Usually, such heterodentate Schiff bases can be synthesized by condensing the aldehydes or ketones with various simple or substituted amines or amino acids[13,14]. ONNO Schiff base ligands derived from salicylaldehyde and diamines are known[15-16]. Dialdehyde or diketones and amine or amino acids have also been utilized to obtain a verity of N_2O_2 Schiff base ligands[17].

The combination of two different ketones with a diamine is expected to give new type of tetradentate N2O2 donor ligands with diverse donor characteristics. However, a vigilant literature survey revealed that Schiff base derived from the combination of methylacetoacetate and acetoacetanilide with ethylenediamine and its coordination behaviour towards the transition metal ions has not been studied yet.

The current chapter describes the synthesis and characteristic description of a tetradentate N2O2 Schiff base derived from the condensation of methylacetoacetate and acetoacetanilide with 1,2-ethylenediamene and its complexes of VO(II), Cr(III), Fe(III), Co(II), Ni(II), Cu(II), Zn(II) and Cd(II). The ligand described in this chapter can act as a dianionic tetradentate donor. The characterization was done based on elemental analysis, magnetic moment measurements, molar conductance, IR, ^1H NMR and electronic spectral data.

A. EXPERIMENTAL

1. Materials and methods

For the preparation of the ligand, methylacetoacetate, acetoacetanilide and ethylenedaimene were used. The transition metal salts used in this study were of BDH AnalaR quality. Mainly chlorides and sulphates of VO(II), Cr(III), Fe(III), Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) were used for the synthesis of complexes.

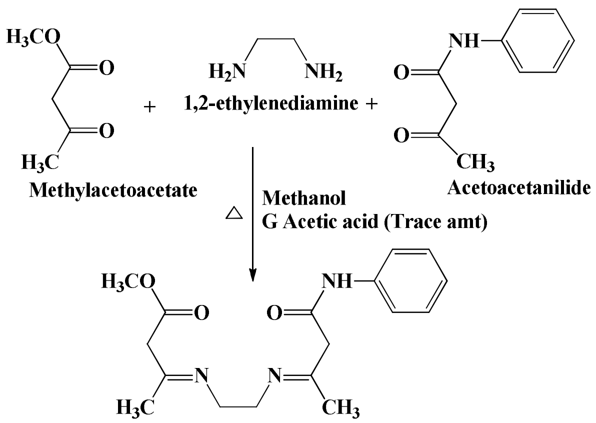
The solvents used for the synthesis, extraction and recrystalization of the ligands and the complexes were ethanol, methanol, chloroform, DMSO, DMF, petroleum benzene, diethyl ether, etc. Commercially available solvents, like methanol and ethanol were purified by standard methods[1-3]. Others were E. Merck reagents and were used as such. The solvents, such as methanol and dimethyl formamide used for spectral and conductivity measurements were of spectroscopic grade.

2. Synthesis

a. Acetoacetanilide-(1,2-ethylenediimie)methylacetoacetate (AcEM)

A mixture of methylacetoacetate (0.025 mol) and acetoacetanilide (0.025 mol) in minimum amount of methanol was added to ethylenediamine (0.025 mol) in methanol in a 250 ml round bottom flask. The mixture was refluxed for 2 h. Completion of the reaction was confirmed by thin-layer chromatographic (TLC) studies on a pre-coated silica gel F_{254} plates from Merck. After completion of the reaction, the mixture was slowly cooled in ice bath. Off-white crystals were formed. The product was filtered and washed with ethanol and dried over anhydrous calcium chloride. (**Scheme. 1**)

Scheme.1: Scheme of the synthesis of the ligand, acetoacetanilide-(1,2-ethylenediimine)methylacetoacetate (AcEM)



***The systematic name of the compound is: (E)-methyl-3-((2-((E)-(4-oxo-4-(phenylamino)butan-2-ylidene)amino)ethyl)imino)butanoate. But for the sake of convenience the name 'Acetoacetanilide-(1, 2-ethylenediimin)methylacetoacetate' and the short form 'AcEM' are adopted in this thesis.**

b. Complexes

The complexes were prepared by a general method. Methanolic solution of the metal salt (0.005 mol in 20 ml ethanol) was added to a solution of the ligand (0.005 mol in 20 ml DMSO) and the mixture was refluxed for about 4 h. It was then cooled and allowed to evaporate the solvent to half of the original volume. The solid complexes formed were filtered off and washed with petroleum benzene and finally with methanol. They were dried over anhydrous calcium chloride. (**Table. 1**)

Table. 1, Physical properties of the synthesized metal complexes			
Si. No	**Metal complex synthesized**	**Color**	**Melting point**
1.	VO(II)	Light brown	285°C
2.	Cr(III)	Light Green	<300°C
3.	Mn(II)	Light Brown	<300°C
4.	Fe(III)	Red	275°C
5.	Co(II)	Light red	278°C
6.	Ni(II)	Yellow-Brown	2700C
7.	Cu(II)	Light Blue	2850C
8.	Zn(II)	White	<3000C
9.	Cd(II)	White	<3000C

B. RESULTS AND DISCUSSION

The data obtained from the analytical- and physico-chemical studies have been correlated to explain the properties, structure and bonding of the compounds.

1. Characterization of the ligand

The ligand derived from the condensation of methylacetoacetate and acetoacetanilide with 1, 2-ethylenediamine was an off-white colored crystals, soluble in non-polar solvents like DMSO, benzene, etc. The homogeneity and purity of the ligand were tested by TLC technique. Melting point (178^0C) of the ligand was determined using a Fisher-Johns apparatus. The ligand was characterized by elemental analysis and by IR, ^{1}H NMR and UV-Vis spectral studies.

a. Elemental analysis

The ligand was subjected to elemental analysis on a CHN-O instrument. The experimentally found out- and calculated percentages of C, H and N were in good agreement, confirming a molecular formula, $C_{17}H_{23}N_3O_3$, for the Schiff base, AcEM. (**Table. 2**)

Table. 2: Elemental analysis of the ligand AcEM						
Ligand	**Carbon (%)**		**Hydrogen (%)**		**Nitrogen (%)**	
	Found	**Calculated**	**Found**	**Calculated**	**Found**	**Calculated**
$C_{17}H_{23}N_3O_3$	63.95	64.33	6.99	7.30	13.01	13.24

b. ^{1}H NMR spectrum

The ^{1}H NMR spectrum of the ligand, AcEE was recorded in DMSO-d_6. The spectrum showed a number of peaks that were characteristic of the compound[18,19]. A sharp singlet at δ value, 9.25 ppm may be assigned to the -NH proton of acetoacetanilide moiety. The signals observed in the range 7.62-7.43 ppm may be assigned to different types of aromatic protons. The singlets at 3.34 and 3.36 ppm, may be attributed to the active methylene protons of acetoacetanilide- and ethylacetoacetate moieties, respectively. A singlet appeared at 4.15 ppm was due to the $-CH_3$ protons of the methoxy group of ethylacetoacetate moiety. The triplet appeared at 2.66 ppm may be assigned to the methylinic protons of diimine moiety of the ligand. The inductive effects of the nitrogen atoms may be responsible for the higher value. A singlet appeared at 1.91 ppm may be assigned to the $-CH_3$ protons of either sides of imine group. **(Fig. 1 &Table. 3)**

Fig. 1: ^{1}H NMR spectrum of ligand, AcEM

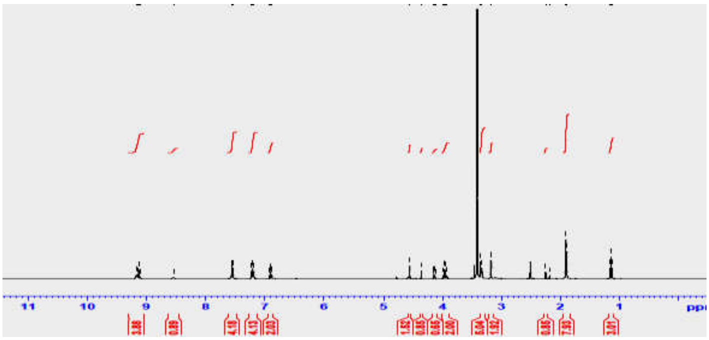


Table. 3, ^{1}H NMR data of ligand, AcEM		
Si.No	**Chemical shift (ppm)**	**Assignment**
1.	9.25 (s)*	-NH proton
2.	7.62 -7.43 (m)	Aromatic protons
3.	3.34 (s)	-CH_2 active methylene proton of acetanilide
4.	3.36 (s)	-CH_2 active methylene proton
5.	4.15 (s)	-CH_3 proton of –OCH_3
6.	4.66 (t)	two -CH_2 protons of imine group
7.	1.91 (s)	-CH_3 proton of either side of imine group
*s= singlet, t= triplet, q= quartet		

c. Infra red spectrum

The IR spectrum of the ligand, AcEM showed a number of absorption bands, which were characteristics of various functional groups present in it. Assignments were made on the basis of analogous compounds known earlier[20,21]. The probable assignments are given in the **Table. 4**. The IR spectrum of the ligand showed a medium intensity band at 3140 and a strong one at 1650 cm^{-1} characteristic stretching of –NH- and >C=O of amide group (-CO-NH-), respectively.

The bands present at 1619 and 1244 cm^{-1} were assigned to the $\nu_{–C=N}$ and $\nu_{=N-C-}$, respectively. The band at 3063 cm^{-1} may be assigned to the aromatic –CH stretching and that at 2905 cm^{-1} to the –CH stretching of the methylene group.

The bands at 2967 and 2939 cm^{-1} were, respectively, due to the symmetric- and asymmetric stretching vibrations of CH_2 group. A sharp band at 1648 cm^{-1} may be due to $\nu_{C=O}$ of ethylacetoacetate moiety. The characteristic bands due to the stretching of –C=O in the acetoacetanilide and ethylacetoacetate, in the range, 1660-1668 cm^{-1} were not present in the spectrum, which indicated the complete condensation of the carbonyl compounds with the diamine. A sharp band at 1211 cm^{-1} may be due to the ν_{C-O} of the ethoxy group. **(Table. 4 & Fig. 2)**

Fig. 2: IR spectrum of the ligand, AcEM

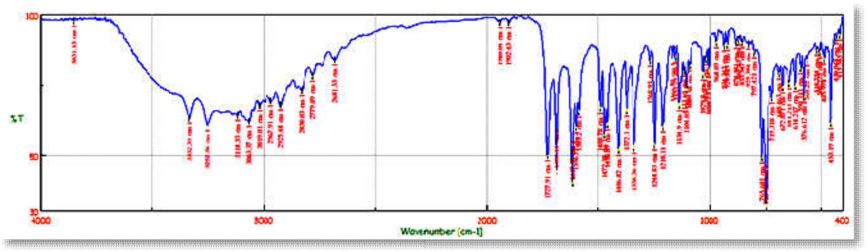


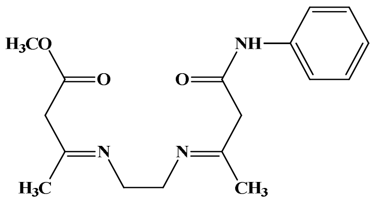
Table. 4 : Significant IR bands of AcEM and their assignments	
Band frequency* (cm^{-1})	**Assignment**
3140 1650	**ν_{-NH} amide $\nu_{-C=O}$ amide**
1619	**$\nu_{>C=N}$ methylacetoacetate**
1648	**>C=O (keto)**
3063 2905	**ν aromatic –CH ν_{-CH2} (Methylene)**
1244	**$\nu_{>C-N-}$**
1616 1559	**δ in plane –CH (aromatic)**
1211	**ν –CO- (ethoxy)**
874 819	**δ out of plane –CH (aromatic)**

d. Electronic spectrum

The electronic spectrum of the ligand, AcEM was recorded in DMSO. The peak at 36363 cm^{-1} may be attributed to π → π* transition of aromatic part of the ligand. A peak at 24310 cm^{-1} may be due to the n → π* transition of the non-bonding electrons present on the oxygen of the keto (>C=O) groups those on the and nitrogen of the azomethine (C=N) groups in the ligands[22].

From the above data, we confirmed that the structure of the ligand, AcEM as shown below (**Fig. 3**)

Fig. 3: Structure of the ligand, AcEM (L2H)



2. Characterization of metal complexes

a. Analytical data of complexes

All the AcEM complexes were found to be colored [except those Zn(II), Cd(II) and Hg(II)], non-hygroscopic and photo-stable. They were soluble in DMF and DMSO but their solubility was very low in common organic solvents. From the data obtained from analytical- and molar conductance (in DMF) studies, the formulae of the complexes have been assigned (**Table. 5**). Aqua complexes were obtained when Cr(III), Mn(II) Co(II) and Ni(II) salts were treated with the ligand.

Table. 5: Analytical data of complexes

Empirical Formula	F*. Wt	Elemental %, Found (Calculated)				
		M	C	H	N	Anion
(VO) $C_{17}H_{21}N_3O_3$	383	12.81 (13.26)	54.01 (53.13)	5.56 (6.00)	11.01 (10.93)	
$CrC_{17}H_{23}N_3O_4Cl$	422	13.01 (12.30)	47.01 (48.29)	6.04 (5.96)	10.36 (9.94)	9.05 (8.15)
$MnC_{17}H_{25}N_3O_5$	408	13.45 (13.07)	51.00 (50.00)	7.00 (6.66)	10.99 (10.29)	----
$FeC_{17}H_{23}N_3O_3Cl_3$	481	11.00 (11.60)	43.06 (42.40)	6.00 (5.23)	7.99 (8.71)	21.56 (22.18)
$CoC_{17}H_{25}N_3O_5$	412	13.85 (14.29)	50.03 (49.52)	6.23 (6.60)	10.58 (10.19)	---
$NiC_{17}H_{25}N_3O_5$	412	15.02 (14.24)	50.43 (49.55)	7.05 (6.60)	11.01 (10.20)	---
$CuC_{17}H_{21}N_3O_3$	378	12.00 (11.03)	54.01 (53.60)	5.95 (6.09)	10.05 (11.03)	---
$ZnC_{17}H_{21}N_3O_3$	379	18.01 (17.17)	52.99 (53.63)	5.02 (5.56)	10.60 (11.04)	---
$CdC_{17}H_{21}N_3O_3$	427	2 5.06 (26.28)	48.00 (47.73)	6.00 (4.95)	8.01 (9.82)	---

b. Molar conductance data

The molar conductances of the complexes at room temperature were determined using their 10^{-3} M solutions in DMSO and are given in the **Table. 6**. The molar conductance values were in the range, 13-50 $\Omega^{-1}mol^{-1}cm^{2}$, indicating the non-electrolytic nature of the complexes and accordingly, they were assigned formulae. Analytical data and spectral studies also supported the suggested formulae.

Table .6: Molar Conductance of AcEM complexes in DMSO

Si No:	Complexes	Λ_m ($\Omega^{-1}mol^{-1}cm^{2}$)
1.	[(VOL]	47
2.	$[CrL(H_2O)Cl]$	30
3.	$[MnL(H_2O)_2]$	25
4.	$[Fe(L2H)Cl_3]$	50
5.	$[CoL(H_2O)_2]$	29
6.	$[NiL(H_2O)_2]$	40
7.	[CuL]	29
8.	[ZnL]	13
9.	[CdL]	31
$L = C_{17}H_{21}N_3O_3$		

c. Magnetic moment data

The magnetic susceptibilities of the complexes were measured using a Gouy balance at room temperature. $Hg[Co(NCS)_4]$ was used as calibarant. Diamagnetic corrections were applied using Pascal constants for atoms and structural units of the complexes. The magnetic susceptibilities, diamagnetic corrections and the effective magnetic moment values were calculated. The corrected magnetic moments are given in the **Table. 7**

The [VOL] complex exhibited a μ_{eff} value of 1.71 B.M., which was very close to the spin-only value for d^1 case[23]. This indicated that the compound was monomeric and without any intermolecular association in the solid state. The AcEM Schiff base complex of Cr(III) showed a magnetic moment value at 3.88 B.M., which indicated its octahedral geometry.

In the present case, $[MnL(H_2O)_2]$ complex showed a value at 5.70 B.M indicating its octahedral geometry[24-26]. $[Fe(L2H)(Cl)_3]$ complex registered a magnetic moment value of 3.93 B.M. This low magnetic moment of this complex may be due to its square pyramidal geometry[33-35].

$[CoL(H_2O)_2]$ registered a magnetic moment of 4.69 B.M. This value indicated its octahedral geometry. The AcEM Schiff base complex of Ni(II) investigated here registered a magnetic moment value of 3.33 B.M., indicating its octahedral geometry. In the present investigation, AcEM Schiff base complex of Cu(II) registered a magnetic moment value at 2.02 B.M., indicating its tetrahedral geometry. (**Table. 7**)

Table. 7: Magnetic moment data of complexes

Si No:	Complexes	μ_{eff} (B.M)*
1.	[(VOL]	1.71
2.	$[CrL(H_2O)Cl]$	3.88
3.	$[MnL(H_2O)_2]$	5.70
4.	$[Fe(L2H)Cl_3]$	3.93
5.	$[CoL(H_2O)_2]$	4.69
6.	$[NiL(H_2O)_2]$	3.33
7.	[CuL]	2.02

*μ_{eff} = Effective magnetic moment, B.M = Bohr magneton

d. Electronic spectra

The electronic spectrum of the [VOL] exhibited bands at 13,600, 19,580 and 24,350cm^{-1}, which were assignable to transitions, $^2B_2 \rightarrow ^2E$ (ν_1), $^2B \rightarrow_2 {}^2B_1$ (ν_2), and $^2B_2 \rightarrow ^2A_1$ (ν_3), respectively. The structure of this 5- coordinate mononuclear complex can be ascribed as tetragonal pyramid[27]. The value of the magnetic moment for this complex was 1.71 B.M. It indicated the presence of one unpaired electron in the complex[59]. In the spectrum of the Cr(III) complex investigated here, two band were observed at 17,150 and 22,420 cm^{-1} and were assigned, respectively, to $^4A_{2g} \rightarrow {}^4T_1$ and the $^4A_{2g} \rightarrow {}^4T_{2g}$ transitions characteristic of an octahedral Cr(III) complex. Octahedral environment of Cr(III) complex, exhibited a third transition corresponding $^4A_{2g} \rightarrow\ ^4T_{1g}$ (P) above 30500 cm $^{-1}$ but in this region the n→π* and π→π* intraligand bands are also observed.[28-30].

The spectrum of Mn(II) complexes show bands around 18,000 - 25,000 cm^{-1} which are assigned to d-d transitions. The light brown coloured [MnL(H_2O)$_2$] exhibited bands at 18,620, 22,950 and 24,910 cm^{-1}which were assigned, respectively, to $^6A_{1g} \rightarrow\ ^4T_{1g}$, $^6A_{1g} \rightarrow\ ^4T_{2g}$ and $^6A_{1g} \rightarrow\ ^4E_g$ transitions of an octahedral Mn(II) complex[30].

Most of the electronic transitions of Fe(III) are at very high energy region and they give no information about the type of bands involving in charge-transfer. The whole interpretation and precise analysis become possible only by a full quantum mechanical analysis of the molecule. In the present investigation, [Fe(L2H)Cl_3] registered two bands, one at 25,300 cm^{-1} and a broad band at 19,700 cm^{-1}, and registered a magnetic moment value of 3.93 B.M. This low magnetic moment value of this complex indicated its square pyramidal geometry.

In the present investigation, the spectrum of Co(II) AcEM complex showed bands at 8,900, 14,900 and 24,400 cm^{-1} and were assigned, respectively, to $^4T_{1g}\rightarrow\ ^4T_{2g}$ (ν_1), $^4T_{1g}\rightarrow\ ^4A_{2g}$ (ν_1) and $^4T_{1g}\rightarrow\ ^4T_{1g}$ (P) (ν_1)[31] transitions of an octahedral Co(II) complex.

The Ni(II) complex, investigated here exhibited three transitions corresponding to octahedral geometry. Bands were identified at 8,610, 13,700 and 24,400 cm^{-1} and were assigned, respectively, to $^3A_{2g}\rightarrow\ ^3T_{2g}$ (F), $^3A_{2g}\rightarrow\ ^3T_{1g}$(F) and $^3A_{2g}\rightarrow\ ^3T_{1g}$ (P) transitions. The ratio of wave numbers of the transition assigned as $^3A_{2g}\rightarrow\ ^3T_{2g}$ (F) and $^3A_{2g}\rightarrow\ ^3T_{1g}$(F) was found to be 1.6, confirming octahedral geometry of the complex.

The hexa-coordinate Cu(II) belongs to the d^9 system. It is susceptible to the Jhan-Teller distortion. A single absorption band representing the transition, $^2E_g\rightarrow\ ^2T_{2g}$ in octahedral and $^2T_2 \rightarrow\ ^2E$ in tetrahedral geometry (10Dq) is expected. The pale blue [Cu(H_2O)$_6$]Cl_2 shows a broad band with two maxima at 9,400 and

12,600 cm^{-1}. The mean value of the two maxima, ie., 11,000 cm^{-1}, is taken as 10 Dq. In the present investigation, the spectrum of Cu(II) AcEM complex exhibited an intense transition at 13,450 cm^{-1} and was assigned to $^2T_2 \rightarrow {}^2E$ [64] transition indicating its tetrahedral geometry. (**Table. 8**)

Table. 8: Electronic spectra of AcEM metal complexes

Si. No:	Complexes	Bands (cm^{-1})	Assignments	Geometry
1.	[(VOL]	13,600	$^2B_2 \rightarrow {}^2E$	Tetragonal Pyramid
		19,580	$^2B_2 \rightarrow {}^2B_1$	
		24,350	$^2B_2 \rightarrow {}^2A_1$	
2.	[CrL(H_2O)Cl]	17,150	$^4A_{2g} \rightarrow {}^4T_1$ (P)	Octahedral
		22,420	$^4A_{2g} \rightarrow {}^4T_{2g}$	
3.	[MnL(H_2O)$_2$]	18,620	$^6A_{1g} \rightarrow {}^4T_{1g}$	Octahedral
		22,950	$^6A_{1g} \rightarrow {}^4T_{2g}$	
		24,910	$^6A_{1g} \rightarrow {}^4E_g$	
4.	[Fe(L2H)Cl_3]	19,700	$^6A_{1g} \rightarrow {}^4T_{2g}$	Square pyramidal
		25,300	CT	
5.	[CoL(H_2O)$_2$]	8,900	$^4T_{1g} \rightarrow {}^4T_{2g}$	Octahedral
		14,900	$^4T_{1g} \rightarrow {}^4A_{2g}$	
		24,400	$^4T_{1g} \rightarrow {}^4T_{1g}$ (P)	
6.	[NiL(H_2O)$_2$]	8,610	$^3A_{2g} \rightarrow {}^3T_{2g}$	Octahedral
		13,700	$^3A_{2g} \rightarrow {}^3T_{1g}$	
		24,400	$^3A_{2g} \rightarrow {}^3T_{1g}$	
7.	[CuL]	13,450 b	$^2T_2 \rightarrow {}^2E$	Tetrahedral

e. IR spectra

The spectra of the complexes showed a number of absorption bands which were characteristic of various functional groups present in it. Assignments have been made on the basis of spectra of analogous compounds known structures[20,21]. The probable assignments are given in the **Table. 9**. The IR spectrum of ligand showed a medium intensity band at 3140 and a strong one at 1650 cm^{-1}, due to $\mathbf{v}_{\mathbf{-NH-}}$ and $\mathbf{v}_{\mathbf{-C=O}}$ of amide group (-CO-NH-), respectively. The band at 1650 cm^{-1} was absent in the spectra of all the complexes except that of [Fe(L2H)Cl_3]. Such a change indicted that the amide group was absent in complexes and the -C=O group of –NH-CO- (amide group) of acetoacetanilide moiety might have participated in the complexation through the enolization of –

CH_2-C=O to –CH=C-OH and subsequent coordination through the deprotonated oxygen in all the complexes except [Fe(L2H)Cl_3]. The above observation was supported by the appearance of new bands around 1124 cm^{-1} due to **ν-c-o** in the spectra of all the complexes.

Band of medium intensity at 1619 cm^{-1} in the spectrum of ligand may be assigned to $\mathbf{\nu_{C=N}}$. However, the spectra of all the complexes, this band was found to be shifted to a lower frequency region by a few cm^{-1} indicating the participation of azomethine nitrogen in coordination.

Disappearance of $\nu_{>C=O}$ band (1648 cm^{-1}) in the spectra of all the complexes, except in that of Fe(III) complex, indicated that the chelation took place through the deprotonated enolic oxygen (methylacetoacetate moety). In the spectra of the all complexes except that of [Fe(LH_2)Cl_3], new bands were observed in the range, 1124 -1110 cm^{-1} due to $\mathbf{\nu\text{-}_{C\text{-}O\text{-}}}$, indicating the enolization of –CH_2-C=O to –CH=C-OH and subsequent coordination through the deprotonated oxygen of methylacetoacetate part. From the above observations, it was clear that the ligand, AcEM coordinated with Fe in [Fe(L2H)Cl_3] complex in a neutral bidentate mode through the azomethine nitrogen atoms.

The band at 3063 cm^{-1} may be assigned to the aromatic –CH stretching and that at 2905 cm^{-1} to the –CH stretching of the methylene group. Sharp bands at the range 1210 -1050 cm^{-1} were due to the $\mathbf{\nu_{C\text{-}O}}$ of methoxy group.

A characteristic sharp band in the spectrum of VO(II) complex at 955 cm^{-1} has been assigned to $\mathbf{\nu_{(V=O)}}$[32]. Broad bands at ~ 3500-3415 cm^{-1} in the spectra of Cr(III), Mn(II) and Ni(II) were attributed to the hydroxyl stretching modes of water molecules. In addition , strong bands at ~ 864-973 and ~ 660 cm^{-1} suggested that the water molecules were coordinated ones.[30] Medium bands around 530 and 450 cm^{-1} in the spectra all the complexes may be assigned[31] to $\mathbf{\nu_{(M\text{-}N)}}$ and $\mathbf{\nu_{(M\text{-}O)}}$, respectively. Bands at 410 cm^{-1} and 415 cm^{-1} in the spectra of

Cr(III) and Fe(III) complexes indicated the presence of M-Cl bonds in these complexes. (**Table. 9& Fig. 4-7**)

Table. 9: Significant IR bands of AcEM and its metal complexes and their assignments

Compounds	Assignments and band frequencies (cm^{-1})							
	$\nu_{\text{-C=O}}$	$\nu_{\text{-C=N}}$	ν-amide	$\nu_{\text{-OH}}$ (H_2O)	$\nu_{\text{=C-O}}$ (enolised)	$\nu_{\text{-M-N}}$	$\nu_{\text{-M-O}}$	$\nu_{\text{-M-Cl}}$
AcEM (LH_2)	1648	1619	3140 1650	---	----	-----	---	----
[(VOL]	1124		3141 ---	----	1119, 1033	495	444	----
[CrL(H_2O)Cl]	1120	1601	3140 ---	3441	1119, 1033	517	445	410
[MnL(H_2O)$_2$]	1112	1600	3144 ---	3307	1112, 1045	505	440	---
[Fe(L2H)Cl_3]	1648	1609	3140, 1648	---	----	510	---	415
[CoL(H_2O)$_2$]	1115	1608	3142 ----	3456	1122, 1056	579	470	----
[NiL(H_2O)$_2$]	1124	1610	3140 ----	3347	1139, 1098	570	465	---
[CuL]	1112	1606	3142 ----	----	1114, 1106	528	478	----
[ZnL]	1120	1607	3142 ----	----	1115, 1041	538	473	----
[CdL]	1122	1611	3140 ----	----	1154, 1004	526	468	---

Fig. 4: IR spectrum of Cr(III) complex

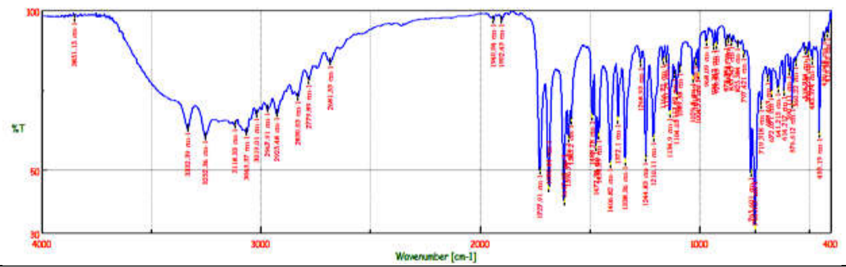


Fig. 5: IR spectrum of Co(II) complex

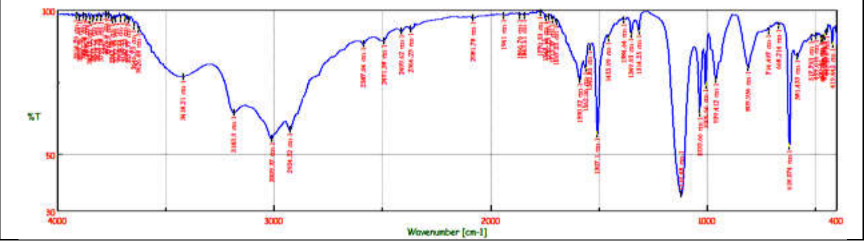


Fig. 6: IR spectrum of Ni(II) complex

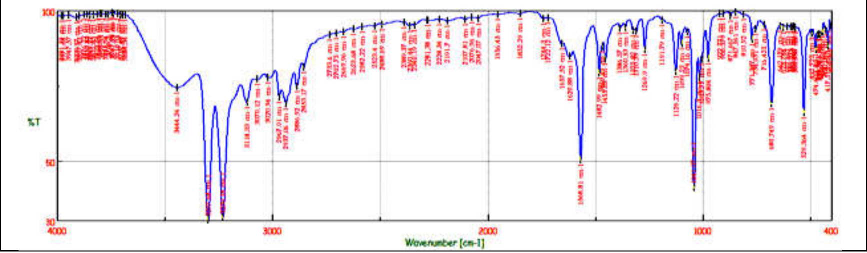
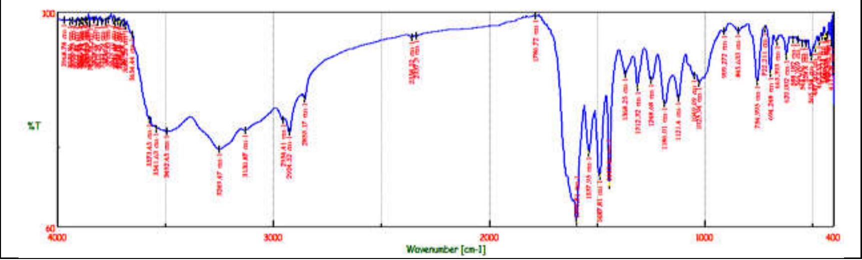


Fig. 7: IR spectrum of Cu(II) complex



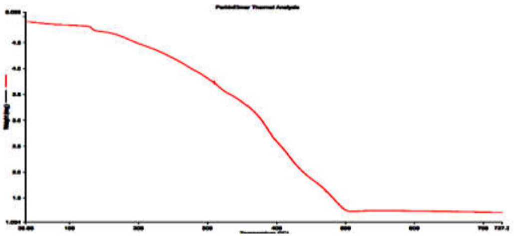
f. Thermal analysis

The thermal decompositions of the Mn(II), Ni(II) and Cu(II) complexes were studied in air. The samples were heated up to 725°C. The TG curve of the Mn(II) and Ni(II) complexes exhibited a mass loss in the range, 150-250°C, indicating the presence of coordinated water molecule in them. (**Table. 10**)

In the case of Mn(II) complex, the first stage of decomposition occurred in the temperature range, 100-150^{0}C, with a mass loss 8.7 % (theoretical 7.0 %). This may be attributed to the removal of the two coordinated water molecule in it.

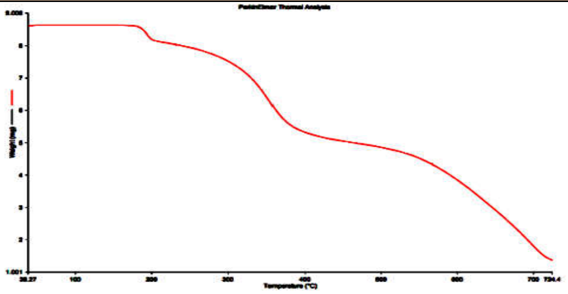
The anhydrous complex showed the second stage of decomposition between 300-375°C with a 30% (theoretical 29 %) mass loss, which may be attributed to the removal of $C_5H_7NO_2$ part of the ligand. The third stage from 500-575°C with mass loss 72 % (theoretical 73%), corresponded to the decomposition of $C_{12}H_{14}N_2O$. The mass of the final residue corresponded to the stable manganese oxide, MnO. **(Fig. 8)**

Fig. 8: TG thermogram of Mn(II) complexes



The thermogram of the Ni(II) complex registered the first mass loss of 8.7 % (theoretical 8.3 %) in the temperature range, 150-200 °C, indicating the mass loss of two coordinated water molecules. The anhydrous complex showed second stage decomposition in the temperature range, 300-400°C with a 31% (theoretical 30 %) mass loss, which may be attributed to the removal of $C_5H_7NO_2$ part of the ligand. The third stage from 675-750 °C with mass loss of 76% (theoretical 77%), corresponded to the decomposition of the remaining part of the ligand, $C_{12}H_{14}N_2O$. The mass of the final residue corresponded to the stable metal oxide, NiO. (**Fig. 9**)

Fig. 9: TG thermogram of Mn(II) complexes



The TG curve of the Cu(II) complex registered a two-stage decomposition. The first stage from 300 to 400 °C with a mass loss of 32 % (theoretical 31%), may be attributed to the decomposition of the part of the ligand, $C_5H_7NO_2$. The next stage, from 650-750 °C with a mass loss of 79% (theoretical 78 %), corresponded to the loss of the remaining part of the ligand, $C_{12}H_{14}N_2O$. The mass of the final residue correspond to the copper oxide, CuO. **(Fig. 10)**

Fig. 10: TG thermogram of Cu(II) complexes

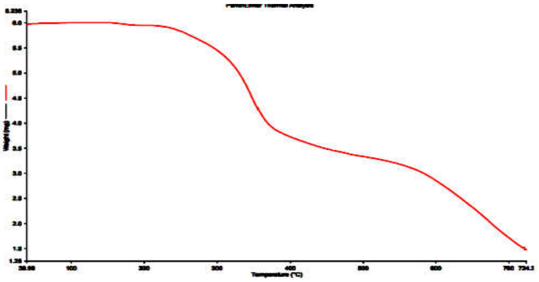


Table. 10: TG data of complexes

Complex	Stage	Temp range in TG (^0C)	Loss of mass in %		Assignment
			TG	Theoretical	
$MnL_2(H_2O)_2$	I Stage	75-150	8.7	7.0	Loss of two H_2O
	II Stage	350-400	30.04	29.0	Loss of $C_5H_7NO_2$
	III Stage	450-550	79.0	81.0	Loss of $C_{12}H_{14}N_2O$ to MnO
$NiL(H_2O)_2$	I Stage	150-200	8.7	8.3	Loss of two H_2O
	II Stage	300-400	31.0	30.05	Loss of $C_5H_7NO_2$
	III Stage	675-750	76.5	74.2	Loss of $C_{12}H_{14}N_2O$ conversion of NiO
CuL	I Stage	300-400	32.0	31.9	Loss of $C_5H_7NO_2$
	II Stage	650-750	79.0	78.0	Loss of $C_{12}H_{14}N_2O$ conversion of CuO

On the basis of the above observations, the probable structures of the AcEM and its metal complexes of VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) are shown below: (**Fig. 11-16**)

Fig. 11: Structure of ligand, AcEM (L2H)	**Fig. 12: Structure of [VOL]**

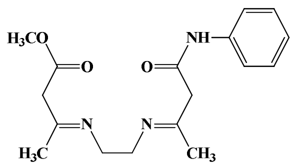
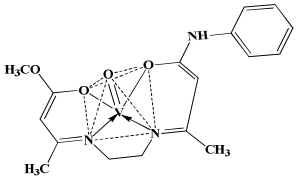

	

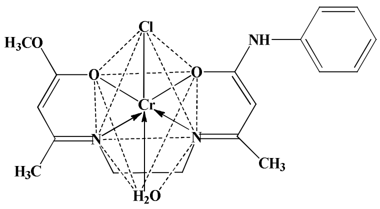
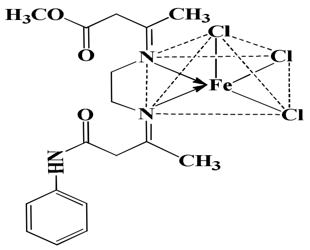
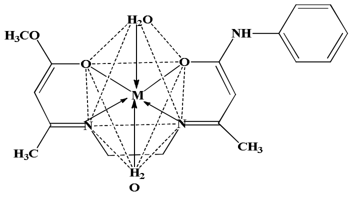
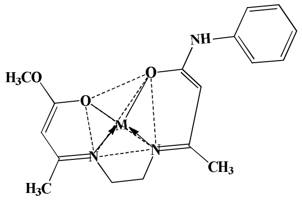
Fig. 13. Structure of [CrL(H_2O)Cl]	**Fig. 14: Structure of [Fe(L2H)(Cl_3)]**
	

Fig. 15: Structure of [ML(H_2O)$_2$], where M = Mn(II), Co(II) and Ni(II)	**Fig. 16: Structure of [ML], where M= Cu(II), Zn(II) and Cd(II)**
	

C. CONCLUSIONS

Coordination complexes of VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) Zn(II) and Cd(II) with a multidentate ONNO donor Schiff base ligand, acetoacetanilide-(1,2-ethylenediimine)methylacetoacetate (L2H) have been prepared and their physico-chemical properties have been studied. The ligand was synthesized by the condensation reaction of acetoacetanilide and methylacetoacetate with 1,2-ethylenediamine in 1:1:1 molar ratio. The complexes have the general formulae, [(VOL], [CrL(H_2O)Cl], [MnL(H_2O)$_2$], [Fe(L2H)Cl_3], [CoL(H_2O)$_2$], [NiL(H_2O)$_2$], [CuL], [ZnL] and [CdL]. Based on the analytical, magnetic- and various spectral studies, geometries have been assigned to these complexes. [(VOL] complex was found to be 5 coordinate tetragonal pyramidal, [CrL(H_2O)Cl], [MnL(H_2O)$_2$], [CoL(H_2O)$_2$] and [NiL(H_2O)$_2$] complexes were found to be octahedral, [Fe(L2H)Cl_3] was found to be square pyramidal and [CuL], [ZnL] and [CdL] complexes were tetrahedral.

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Chapter V

SYNTHESIS AND CHARECTERISATION OF SCHIFF BASE COMPLEXES DERIVED FROM O-VANILLIN AND ACETOACETANILLIDE WITH 1, 2-ETHYLENEDIAMINE

Tetradentate Schiff bases with N_2O_2 donor atoms have been recognized as an important class of chelating ligands for synthesizing medicinally- and catalytically useful metal complexes[1-3]. The flexible donor behavior of these types of chelating ligands could also be useful to generate interesting dimeric and polymeric structures as synthons, a typical supramolecular compound[4,5].

Vanillin is one of the most widely recognized aromatic chemical. Vanillic acid is a well-known product of the degradation of lignin and lignin-related substances by the white-rot fungi and other microorganisms[6]. It was also found to be formed during the dissimilation of ferulic acid by the white-rot fungi and the fungi *imperfecti*[7,8]. *In vivo* anticancer studies using mice have proven the clinical efficacy of vanillin. The colorectal cancer is one of the most common types of cancer. Various chemotherapeutic agents used in the treatment of colorectal cancer produce several adverse effects which are not acceptable by cancer patients. Currently, scientists are investigating the use of natural compounds isolated from plant sources for the treatment of cancer which are found to have only a little adverse effects[9]. Recently, vanillin showed antiplasmodial and antidepressant activity in animal models[10].

We are interested in the synthesis, structural evaluation and coordination chemistry of novel Schiff base ligands derived from vanillin and diamine[11,12]. As a part of our ongoing studies on the structures and properties of polydentate Schiff base ligands, we report in this chapter the synthesis and characterization of

Schiff base derived from the condensation reaction of o-vanillin and acetoacetanilide with 1,2-ethylenediamene and its complexes with VO(II), Cr(II), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II). The characterization was done based on elemental analysis, magnetic moment– and molar conductance measurements, IR, ^{1}H NMR and electronic spectral data.

A. Experimental

1. Materials and methods

For the preparation of the ligand, o-vanillin, acetoacetanilide and 1,2-ethylenedaimene were used. The transition metal salts used in this study were BDH AnalaR quality. Mainly chlorides, sulphates, nitrates or acetates of VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) were used for the synthesis of complexes.

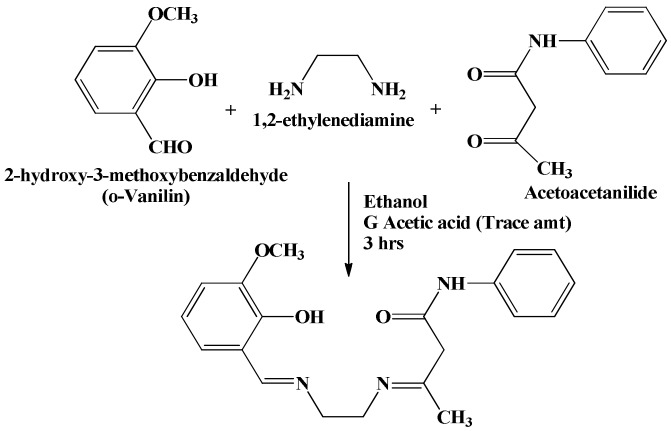
The solvents used for the preparation, extraction and recrystalization of the ligand and the metal complexes were ethanol, methanol, chloroform, DMF, DMSO, petroleum benzene, diethyl ether, etc. Commercially available solvents, like ethanol and methanol were purified by standard methods. Others were E. Merck reagents and were used as such. The solvents, such as methanol and dimethyl formamide used for spectral and conductivity measurements were of spectroscopic grade.

2. Synthesis

a. Ligand, *o*-vanillin-(1,2-ethylenediimine)acetoacetanilide (VEAc)

O-vanillin (0.025 mol) and acetoacetanilide (0.025 mol) were mixed in minimum amount of ethanol and was added to 1, 2-ethylenediamine (0.025 mol) in ethanol in a 250 ml round bottom flask. The mixture was allowed to reflux for 2 h. Completion of the reaction was confirmed by thin-layer chromatographic (TLC) studies on a pre-coated silica gel F_{254} plates from Merck. After the completion of the reaction, the mixture was slowly cooled in an ice bath. The yellow crystals formed were filtered, washed with ethanol and dried over anhydrous calcium chloride. The compound was recrystallized from DMSO. (**Scheme. 1**)

Scheme. 1: Scheme of the preparation of the ligand, VEAc



***The systematic name of the compound is: (E)-3-((2-((E)-(2-hydroxy-3-methoxybenzylidene)amino)ethyl)imino)-N phenylbutanamide. But for the sake of convenience the name 'Ortho-vanillin-(1, 2-ethylenediimin)acetoacetanilide' and the short form 'VEAc' are adopted in this thesis.**

b. Complexes

An ethanolic solution of the metal salt (0.005 mol in 25 ml ethanol) was added to a solution of the ligand (0.005 mol in 25 ml dimethylsulphoxide) and the mixture was allowed to reflux for about 4 h. The reaction mixture was then cooled and the solid complex formed was filtered off, washed several times with petroleum benzene and finally with methanol. The product was dried over anhydrous calcium chloride. (**Table. 1**)

Table. 1: Physical properties of the synthesized complexes			
Si. No	**Metal Salt Used**	**Color**	**Melting point**
1.	**$VOSO_4.H_2O$**	**Dark green**	**285°C**
2.	**$CrCl_3.2H_2O$**	**Green**	**296°C**
3.	**$MnSO_4.5H_2O$**	**Brown**	**<300°C**
4.	**$FeCl_3.6H_2O$**	**Red**	**293°C**
5.	**$CoCl_2.5H_2O$**	**Dark green**	**<300°C**
6.	**$NiCl_2.2H_2O$**	**Dark green**	**298^0C**
7.	**$CuCl_2.2H_2O$**	**Greenish brown**	**275^0C**
8.	**$ZnSO_4.7H_2O$**	**Light yellow**	**265^0C**

B. RESULTS AND DISCUSSION

The data obtained from the analytical- and physico-chemical studies have been interconnected to explain the properties, structure and bonding of the Schiff base ligand and its complexes.

1. Characterization of the ligand

The Schiff base ligand, VEAc was yellow colored crystals, readily soluble in non-polar organic solvents like DMSO, DMF, benzene, etc. The homogeneity and purity of the ligand were confirmed by thin layer chromatographic technique. Melting point (180^0C) of the ligand was determined using a Fisher-Johns apparatus. The ligand was characterized by elemental analysis, IR, ^1H NMR and electronic spectral studies.

a. Elemental analysis

The Schiff base ligand, VEAc was subjected to elemental analysis on a CHN-O instrument. The experimentally found out- and calculated percentages of C, H and N were in good agreement, confirming its molecular formula as, $C_{18}H_{25}N_3O_3$. (**Table. 2**)

Table. 2: Elemental analysis of the ligand, VEAc						
Ligand	**Carbon (%)**		**Hydrogen (%)**		**Nitrogen (%)**	
	Found	**Calculated**	**Found**	**Calculated**	**Found**	**Calculated**
$C_{20}H_{23}N_3O_3$	**66.91**	**67.05**	**5.99**	**6.56**	**12.00**	**11.89**

b. ^{1}H NMR spectrum

^{1}H NMR spectrum of the ligand was recorded in DMSO-d_6. The spectrum showed a number of peaks that are characteristic of the compound[1,17]. A sharp singlet at 9.25 ppm may be assigned to -NH proton of acetoacetanilide. The signals observed in the range, 7.61-7.20 ppm were assigned to the different types of aromatic protons of acetoacetanilide moiety.

A singlet at 3.24 ppm may be attributed to the active methylene protons of acetoacetanilide moiety. There singlets appeared at 3.81 and 4.55 ppm may be attributed to the –OCH_3 and –OH protons, respectively, of the vanillin part. The signals observed in the range 7.04-7.22 ppm may be assigned to the different aromatic protons of o-vanillin moiety. The triplet peaks appeared at 2.88-2.84 ppm range was assigned to the methylinic protons of ethylenediimine moiety of the ligand. A singlet at 1.94 ppm may be attributed to the –CH_3 protons of acetoacetanilide moiety. The –CH=N- proton of o-vanillin moeity appeared at 7.79 ppm. (**Fig. 1** & **Table. 3**)

Fig. 1: ^{1}H NMR spectrum of the ligand, VEAc

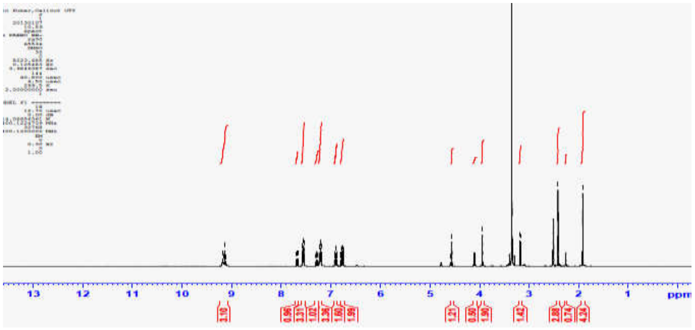


Table. 3: ^{1}H NMR data of ligand, VEAc		
Si. No.	Chemical shift (ppm)	Assignment
1.	9.25 (s)*	-NH proton
2.	7.19-7.61 (m)	Aromatic protons
3.	7.04-7.22 (m)	Aromatic protons
4.	3.83 (s)	-OCH_3 (methoxy) proton
5.	4.55 (s)	-OH proton
7.	2.88-2.84 (t)	-CH_2 protons near imine group
8.	3.24(s)	Active methylene proton
9.	1.94(s)	-CH_3 proton of Acetoacetanilide
*s= singlet, t= triplet, q= quartet		

c. IR spectrum

The infrared spectrum of VEAc showed a number of absorption bands, which were characteristics of various functional groups present in it. Assignments were made on the basis of the spectra of analogous compounds known earlier[18,19]. The probable assignments are given in the **Table. 4**.

The IR spectrum of ligand showed a band of strong intensity at 1649 and one of the medium intensity at 3015 cm^{-1}. They were due to $\nu_{-C=O}$ and ν_{-NH-} of amide group (-CO-NH-), respectively. The bands present at 1623 and 1290 cm^{-1} were assigned to the $\nu_{-C=N}$ and $\nu_{=N-C-}$, respectively. A band at 1638 cm^{-1} may be assigned $\nu_{-C=O}$ of acetoacetanilide moiety. The bands at 3317 and 3110 cm^{-1} may be assigned to the aromatic –CH stretching of first and second phenyl group. The bands at 2967 and 2939 cm^{-1} were, respectively, due to the symmetric- and asymmetric stretching vibrations of CH_2 group. A band at 3317 cm^{-1} was due to ν_{-OH} of vanillin moiety.

The characteristic stretching bands of >C=O of acetoacetanilide and ethylacetoacetate, in the range 1640-1658 cm^{-1} were not present in the spectrum of ligand, which indicated the complete condensation of the carbonyl compounds with the diamine. Sharp bands at 1240 and 1050 cm^{-1} were characteristic of ν_{-O-CH3} (methoxy) group. (**Table. 4 & Fig. 2**)

Fig. 2: IR spectrum of the ligand, VEAc

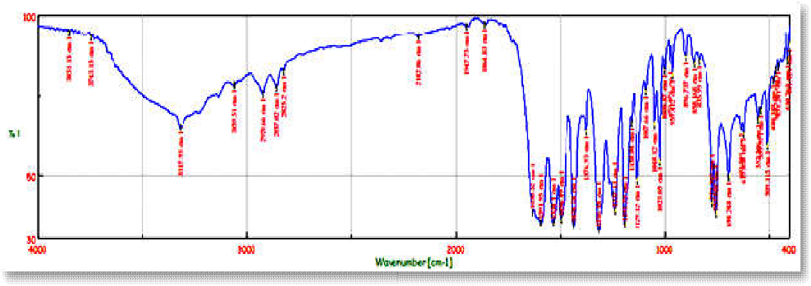


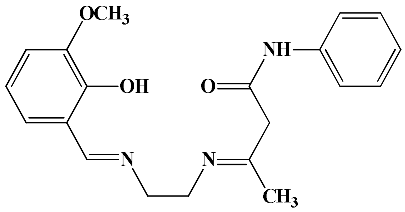
Table. 4: Significant IR bands of ligand, VEAc

Band frequency* (cm^{-1})	Assignment
3015 1649	ν amide-I ν amide-II
3455	Phenolic –OH
1623	$\nu_{>C=N}$
3057 2967	ν aromatic –CH ν_{-CH2} (Methylene)
1290	$\nu_{>C-N-}$
1610 1555	δ in plane –CH (aromatic)
1240 1050	ν_{-CO-} (methoxy)
864 810	δ out of plane –CH (aromatic)

d. Electronic spectrum

The electronic spectrum of the ligand was recorded in DMSO at room temperature. The peak at 34,965 cm^{-1} was attributed to $\pi \rightarrow \pi^*$ transition. It indicated the presence of aromatic part in the ligand. A peak at 22,935 cm^{-1} was due to the $n \rightarrow \pi^*$ transition of the non-bonding electrons present on the oxygen of the keto (>C=O) groups and nitrogen of the azomethine (C=N) groups of the ligand[20]. From the above data, we have confirmed the structure of the ligand, VEAc as shown below. (**Fig. 3**)

Fig. 3: Structure of the ligand, VEAc (L2H)



2. Characterization of complexes

a. Analytical data

All the VEAc complexes were found to be coloured, non-hygroscopic, photo-stable and readily soluble in DMSO and DMF. Based on the data obtained from analytical- and molar conductance (in DMSO) data of the complexes, their formulae were assigned. (**Table. 5**) Aqua complexes were obtained when Cr(III), Mn(II), Fe(III) and Zn(II) salts were treated with the ligand solution. (**Table. 5**)

Table. 5: Analytical data of complexes

Empirical formula	F^*. Wt	Elemental %, Found (Calculated)				
		Metal	C	H	N	Anion
$(VO)C_{20}H_{21}N_3O_3$	418	11.98 (12.18)	56.65 (57.42)	5.55 (5.06)	9.96 (10.04)	
$CrC_{20}H_{23}N_3O_4Cl$	456	12.00 (11.38)	51.01 (52.58)	5.53 (5.07)	10.00 (9.20)	8.04 (7.76)
$MnC_{20}H_{25}N_3O_5$	442	12.01 (12.42)	53.95 (54.30)	5.16 (5.70)	10.01 (9.50)	----
$FeC_{20}H_{23}N_3O_4Cl$	460	11.95 (12.12)	52.00 (52.14)	4.97 (5.03)	8.85 (9.12)	6.98 (7.70)
$CoC_{20}H_{21}N_3O_3$	410	14.11 (14.36)	57.86 (58.54)	4.99 (5.16)	10.88 (10.24)	---
$NiC_{20}H_{21}N_3O_3$	410	13.21 (14.31)	57.11 (58.58)	4.87 (5.16)	11.24 (10.25)	---
$CuC_{20}H_{21}N_3O_3$	414	16.01 (15.31)	56.88 (57.89)	5.65 (5.10)	9.96 (10.13)	---
$ZnC_{20}H_{25}N_3O_5$	425	15.00 (14.44)	53.99 (53.05)	4.88 (5.56)	9.70 (9.28)	---

b. Molar conductance data

The molar conductances at room temperature were determined using 10^{-3} M solutions of the complexes in DMSO and are presented in the **Table. 6**. In DMSO, the molar conductances of complexes were in the low range 11-56 $\Omega^{-1}mol^{-1}cm^{2}$, indicating their non-electrolytic nature and accordingly their formulae have been assigned. Analytical data and spectral studies also supported the suggested formulae.

Table. 6: Molar conductance of complexes in DMSO

Si No:	Complexes	Λ_m ($\Omega^{-1}mol^{-1}cm^{2}$)
1.	[(VOL]	39
2.	[CrL(H_2O)Cl]	30
3.	[MnL(H_2O)$_2$]	18
4.	[Fe(L)(H_2O)Cl]	40
5.	[CoL]	45
6.	[NiL]	56
7.	[CuL]	39
8.	[ZnL(H_2O)$_2$]	50
L = $C_{20}H_{23}N_3O_3$		

c. Magnetic moment data

Magnetic moment measurements and electronic spectroscopy are good methods for investigating the geometry of transition metal complexes. As the complexes usually have partially filled d or f orbitals, a range of magnetic properties are expected, depending on the electronic configuration, oxidation state and coordination number of the central metal.

[VOL] complex of exhibited a μ_{eff} value of 1.74 B.M., which was very close to the spin-only value for one unpaired electron[21]. This indicated that the compound was monomeric. VEAc complexes of Cr(III) and Fe(III) showed magnetic moments of 3.88 and 5.70 B.M., respectively, indicating their octahedral geometries.

The observed magnetic moment values of Mn(II) and Co(II) complexes were 5.8 and 4.9 B.M., indicating their octahedral and tetrahedral geometries, respectively[22-24] Based on the magnetic moments, 3.26 and 2.01 B.M., for the Ni(II) and Cu(II) complexes, respectively, tetrahedral geometries were assigned to them. (**Table. 7**)

Table. 7: Magnetic moment data of complexes		
Si No:	**Complexes**	**μ_{eff} (B.M)**
1.	**[(VOL]**	**1.74**
2.	**$[CrL(H_2O)Cl]$**	**3.88**
3.	**$[MnL(H_2O)_2]$**	**5.80**
4.	**$[Fe(L)(H_2O)Cl]$**	**5.70**
5.	**[CoL]**	**4.90**
6.	**[NiL]**	**3.26**
7.	**[CuL]**	**2.01**

d. Electronic spectra

The electronic spectral data of the complexes can be interpreted in a structural perceptive as follows. [VOL] complex exhibited bands at 13,400, 19,360 and 24,100cm^{-1}, which were assigned to transitions, $^2B_2 \rightarrow {}^2E$ (ν_1), $^2B \rightarrow_2 {}^2B_1$ (ν_2), and $^2B_2 \rightarrow {}^2A_1$ (ν_3), respectively. The geometry of this complex can be assigned as tetragonal pyramidal[52]. The value of the magnetic moment for this complex was 1.74 B.M., which indicated the presence of one unpaired electron in the complex[25].

The electronic transitions of Cr(III) complex investigated here were at 16,900 and 22,100 cm^{-1} which were assigned, respectively, to $^4A_{2g} \rightarrow {}^4T_1$ and $^4A_{2g} \rightarrow {}^4T_{2g}$ transitions in an octahedral geometry. Octahedral Cr(III) complex, showned a third d-d transition corresponding $^4A_{2g} \rightarrow {}^4T_{1g}$ (P) above 30610 cm $^{-1}$ but in this region the n→π* and π→π* intraligand bands are also observed. [26-28].

The spectrum of the Mn(II) complexes exhibit a number weak bands in the region 17,000 - 24,500 cm^{-1} which are assigned to d-d transitions, characteristic of octahedral geometry. The brown color of $[MnL(H_2O)_2]$ and electronic spectral band at 18,500, 22,800 and 24,600 cm^{-1} assigned to $^6A_{1g} \rightarrow {}^4T_{1g}$, $^6A_{1g} \rightarrow {}^4T_{2g}$ and $^6A_{1g} \rightarrow {}^4E_g$ transitions, respectively, indicated its octahedral geometry[28].

In the present investigation, the Fe(III) complex was found to be pale red in color and gave weak bands in the range 25,000 – 20,000 cm^{-1}. These were assigned to charge-transfer transitions of Fe(III) ion in an octahedral field[13,14].

The spectrum of Co(II) complex of VEAc showed intense transitions. Bands were present at 7792, 8110 and 16255 cm^{-1} and were assigned, respectively, to $^4A_2 \rightarrow ^4T_2$ (ν_1), $^4A_2 \rightarrow ^4T_1$ (ν_2) and $^4A_2 \rightarrow ^4T_1$ (P) (ν_3)[15] transitions, typical of an tetrahedral Co(II) complex.

The Ni(II) complex investigated here showed transitions corresponding to tetrahedral geometry. Bands were identified at 7549, 8500 and 14250 cm^{-1} and were assigned, respectively, to $^3T_1 \rightarrow ^3T_2$, $^3T_1 \rightarrow ^3A_2$ and $^3T_1 \rightarrow ^3T_1(P)$[15] transitions.

The 4 coordinate Cu(II) belongs to the d^9 system. In a tetrahedral geometry, we expect a single absorption band representing to the transition, $^2T_2 \rightarrow ^2E$. In the present investigation, the spectrum of the Cu(II) complex exhibited an intense band at 23,800 cm^{-1} and was assigned to the $^2T_2 \rightarrow ^2E$ transition indicating its tetrahedral geometry[15]. (**Table. 8**)

Table. 8: Electronic spectra of complexes

Si. No:	Complexes	Bands (cm^{-1})	Assignments	Geometry
1.	[(VOL]	13,400	$^2B_2 \rightarrow ^2E$	Tetragonal Pyramid
		19,360	$^2B_2 \rightarrow ^2B_1$	
		24,100	$^2B_2 \rightarrow ^2A_1$	
2.	[CrL(H_2O)Cl]	16,900	$^4A_{2g} \rightarrow ^4T_1$ (P)	Octahedral
		22,100	$^4A_{2g} \rightarrow ^4T_{2g}$	
3.	[MnL(H_2O)$_2$]	18,500	$^6A_{1g} \rightarrow ^4T_{1g}$	Octahedral
		22,800	$^6A_{1g} \rightarrow ^4T_{2g}$	
		24,600	$^6A_{1g} \rightarrow ^4E_g$	
4.	[Fe(L)H_2OCl_3]	20,900	$^6A_{1g} \rightarrow ^4T_{2g}$	Octahedral
		24,100	CT	
5.	[CoL(H_2O)$_2$]	7,792	$^4A_2 \rightarrow ^4T_2$	Tetrahedral
		8,110	$^4A_2 \rightarrow ^4T_1$	
		16,255	$^4A_2 \rightarrow ^4T_1(P)$	
6.	[NiL(H_2O)$_2$]	7,549	$^3T_1 \rightarrow ^3T_2$	Tetrahedral
		8,500	$^3T_1 \rightarrow ^3T_2$	
		14,250	$^3T_1 \rightarrow ^3T_1(P)$	
7.	[CuL]	23,800	$^2T_2 \rightarrow ^2E$	Tetrahedral

e. IR spectra

IR spectral technique is quite useful for the identification and characterization of metal complexes and in assigning structures and geometries to them. The probable assignments of IR spectral bands are given in the **Table. 9**. The IR spectrum of ligand showed a medium intensity band at 3015 and a strong one at 1649 cm^{-1}, respectively, due to $\nu_{\text{–NH-}}$ and $\nu_{\text{-C=O}}$ of amide group (-CO-NH-). The band at 1649 cm^{-1} was absent in the spectra of all the complexes. This indicated that the –NH-CO-CH_2- (amide group) of acetoacetanilide moiety has undergone enolisation to –CH=C-OH and after deprotonation coordinated to the metal ion in the complexes. This was supported by the appearance of new bands around 1165 cm^{-1} due to $\nu_{\text{-C-O}}$, in the spectra of the complexes.

A band of medium intensity at 1623 cm^{-1} in the spectrum of ligand may be assigned to $\nu_{C=N}$. However, the spectra of all the complexes, this band was found to be shifted to a lower frequency region by 5 to 10 cm^{-1}, indicating the coordination of azomethine nitrogens.

The bands at 3063 cm^{-1} may be assigned to the aromatic –CH stretching and those at 2905 cm^{-1} to –CH stretching of the methylene group. Sharp bands at 1210 and 1050 cm^{-1} may be assigned as the characteristic peaks of $\nu_{\text{-C-O-CH3}}$ of methoxy group of vanillin moiety.

A band at 3455 cm^{-1} in the spectrum of the ligand may be assigned to the phenolic $\nu_{\text{-OH}}$. However, in the spectra of all the complexes, this band was absent, indicating the coordination of phenolic oxygen after deprotonation.

A characteristic non-ligand sharp band in the spectrum of VO(II) complex at 955 cm^{-1} has been assigned to $\nu_{(V=O)}$[29]. Broad bands ~ 3500-3460 cm^{-1} in the spectra of the Cr(III), Mn(II), Fe(III) and Zn(II) complexes may be assigned to the hydroxyl stretching modes of water molecules. In addition, strong bands ~ 870-980 and ~ 650 cm^{-1} suggested that the water molecules were coordinated[30]. Medium bands around 520 and 430 cm^{-1} in the spectra of all the complexes may be assigned[31] to $\nu_{(M-N)}$ and $\nu_{(M-O)}$, respectively. Bands at 413 and 415 cm^{-1} in the spectra of Cr(III) and Fe(III) complexes indicated the presence of ν_{-M-Cl} bonds in these complexes. (**Table. 9& Fig. 4-7**)

Table. 9: Significant bands in the IR spectra of complexes and their assignments

Compounds	**Assignments and band frequencies (cm^{-1})**						
	$\nu_{-C=N}$	**ν-amide**	ν_{-OH} **(H_2O)**	$\nu_{=C-O}$ **(enolised)**	ν_{-M-N}	ν_{-M-O}	ν_{-M-Cl}
VEAc (LH_2)	**1623**	**3015, 1649**	**3317**	**----**	**-----**	**---**	**----**
[(VOL]	**1605**	**3012** **---**	**----**	**1129, 1040**	**510**	**484**	**----**
[CrL(H_2O)Cl]	**1602**	**3017** **---**	**3441**	**1119, 1033**	**527**	**465**	**413**
[MnL(H_2O)$_2$]	**1610**	**3018** **---**	**3420**	**1122, 1018**	**528**	**470**	**---**
[FeL(H_2O)Cl]	**1605**	**3014** **---**	**3500**	**1146, 1038**	**520**	**485**	**413**
[CoL]	**1608**	**3014** **----**	**-----**	**1123, 1076**	**509**	**482**	**----**
[NiL]	**1605**	**3016** **----**	**----**	**1110, 1090**	**513**	**460**	**---**
[CuL]	**1610**	**3014** **----**	**----**	**1100, 1040**	**528**	**474**	**----**
[ZnL(H_2O)$_2$]	**1602**	**3013** **----**	**3445**	**1124, 1029**	**538**	**468**	**----**

Fig. 4: IR spectrum of VO(II) complex

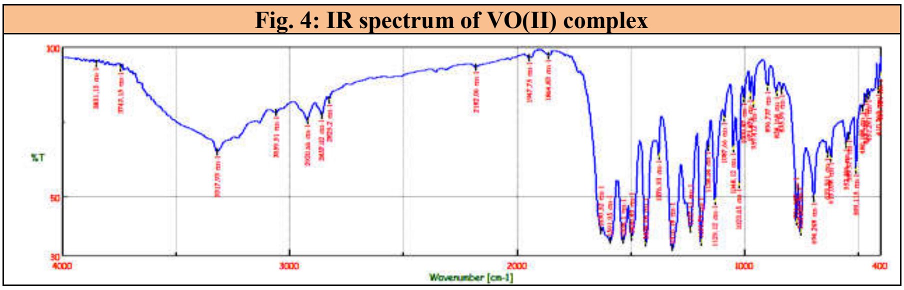


Fig. 5: IR spectrum of Cr(III) complex

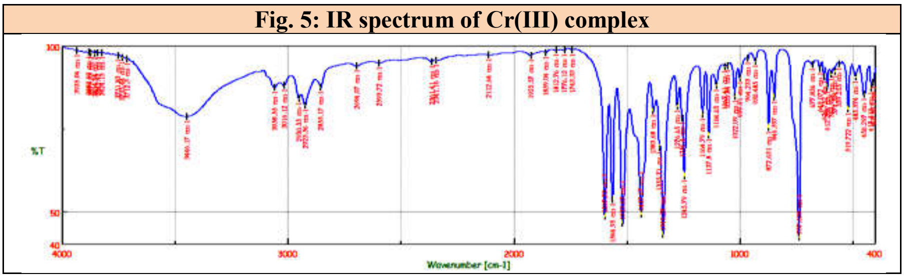


Fig. 6: IR spectrum of Ni(II) complex

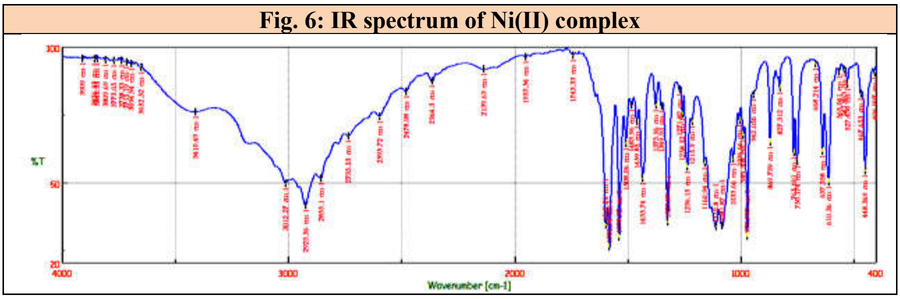
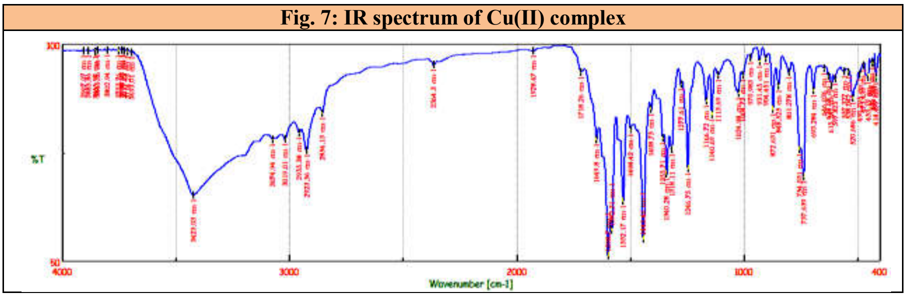


Fig. 7: IR spectrum of Cu(II) complex



On the basis of above observations, the probable structures of the VEAc and its complexes of VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) are shown below: (**Fig. 8-13**)

Fig. 8: Structure of ligand, VEAc	**Fig. 9: Structure of [VOL]**

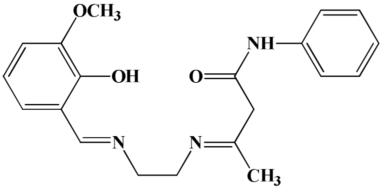
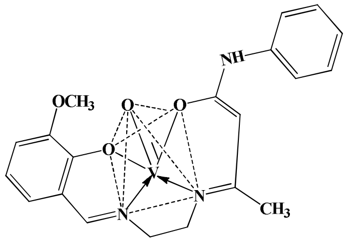

	

Fig. 10. Structure of $[CrL(H_2O)Cl]$	**Fig. 11. Structure of $[FeL(H_2O)Cl]$**

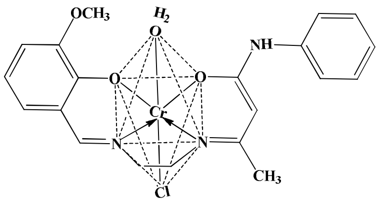
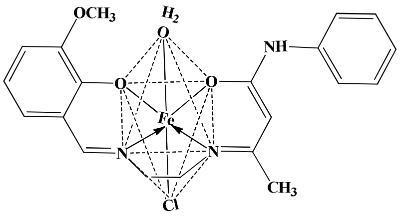
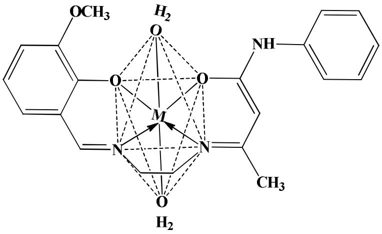
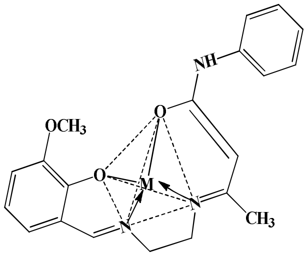

	

Fig. 12: Structure of $[ML(H_2O)_2]$, where M= Mn(II) and Zn(II)	**Fig. 13: Structure of [ML], where M = Co(II), Ni(II) and Cu(II)**
	

C. CONCLUSIONS

Novel Schiff base, o-Vanillin(1,2-ethylenediimine)acetoacetanilide and its VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) complexes were synthesized. The Schiff base synthesized here acted as a tetradentate ONNO ligand. The properties and structures of the ligand and the complexes were determined by the elemental- and spectral analysis. The complexes have the general formulae, [(VO)L], [CrL(H_2O)Cl], [MnL(H_2O)$_2$], [FeL(H_2O)Cl], [CoL], [NiL], [CuL] and [ZnL(H_2O)$_2$]. Based on the analytical-, magnetic- and various spectral studies, geometries have been assigned to these complexes. [(VO)L] was found to be tetragonal pyramidal, [CrL(H_2O)Cl], [MnL(H_2O)$_2$], [FeL(H_2O)Cl] and [ZnL(H_2O)$_2$] were octahedral and [CoL], [NiL] and [CuL] were tetrahedral.

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Chapter VI

SYNTHESIS AND CHARECTERISATION OF SCHIFF BASE COMPLEXES DERIVED FROM O-HYDROXYACETOPHENONE AND ACETOACETANILIDE WITH 1, 2-ETHYLENEDIAMINE

The synthesis and characterization of nitrogen and oxygen donor ligands has emerged as one of the main research areas in coordination chemistry[1-5]. Schiff bases are an important class of organic ligands that can coordinate to a metal through their different donor atoms, which has led to the formation of a variety of coordination compounds[6-15]. These metal complexes exhibit in diverse fields such as interesting structures and geometries. Therefore, these complexes have numerous applications[16-20], biological-[21-25], analytical-[26] and industrial fields[27-31].

In the present work, we synthesized a Schiff base ligand, derived from *o*-hydroxyacetophenone, acetoacetanilide and 1,2-ethylenediamine and its complexes. The ligand was characterized analytically and spectroscopically by elemental analysis, IR-, ^{1}H NMR- and UV spectral techniques. The physico-chemical methods like elemental analysis, magnetic susceptibility and IR- and UV spectral measurements were employed for the characterization of the complexes.

A. EXPERIMENTAL

1. Materials and methods

For the preparation of the ligand, o-hydroxyacetophenone, acetoacetanilide and 1,2-ethylenedaimene were used. The metal salts used in this study were of BDH AnalaR quality. Mainly chlorides and sulphates of VO(II), Cr(III), Mn(II), Fe(III), Co(III), Ni(II), Cu(II) and Zn(II) were used for the synthesis of complexes.

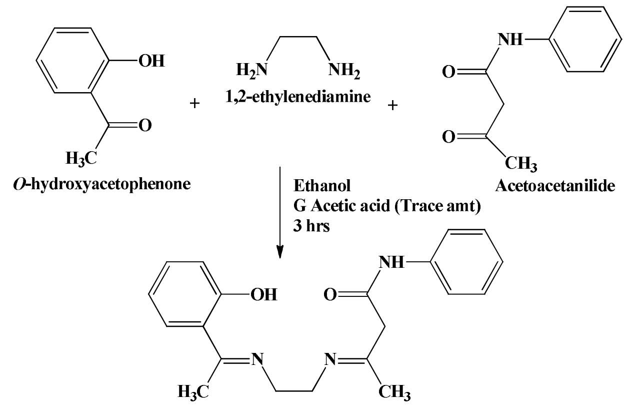
The solvents used for the synthesis, extraction and recrystalization of the ligands and the complexes were ethanol, methanol, chloroform, DMF, DMSO, petroleum benzene, diethyl ether, etc. Commercially available solvents, like ethanol and methanol were purified by standard methods[32]. Others were E. Merck reagent grade and were used as such. The solvents, such as methanol and dimethyl formamide used for spectral and conductivity measurements were of spectroscopic grade.

2. Synthesis

a. *o*-Hydroxyacetophenone-(1,2-ethylenediimine)acetoacetanilide (HEAc)

o-Hydroxyacetophenone (0.025 mol) and acetoacetanilide (0.025 mol) in minimum amount of methanol were added to 1,2-ethylenediamine (0.025 mol) in methanol in a 250 ml round bottom flask. Added a few drops of mineral acid as dehydrating agent. The mixture was allowed to reflux for 2 h. After the completion of the reaction, the mixture was cooled in an ice bath till the yellow crystals separated. Completion of the reaction was confirmed by thin-layer chromatographic (TLC) studies on a pre-coated silica gel F_{254} plate from Merck. The product was filtered, washed with ethanol and dried over anhydrous $CaCl_2$. **(Scheme. 1**

Scheme.1: Synthesis of ligand, HEAc



***The systematic name of the compound is: (E)-3-((2-((E)-(1-(2-hydroxyphenyl)ethylidene)amino)ethyl)imino)-N-phenylbutanamide. But for the sake of convenience the name 'Ortho-hydroxyacetophenone-(1, 2-ethylenediimine)acetoacetanilide' and the short form 'HEAc' are adopted in this thesis**

b. Complexes

Ethanolic solution of the metal salt (0.005 mol in 20 ml ethanol) was added to a solution of the ligand (0.005 mol in 20 ml DMSO) and the mixture was refluxed for about 4 h. It was then cooled and allowed to evaporate the solvent to reduce approximately half of the total volume. The solid complexes formed were filtered off, washed several times with petroleum benzene and finally with methanol and were dried over anhydrous calcium chloride. (**Table. 1**)

Table. 1: Physical properties of the synthesized metal complexes

Si. No	Metal Salt Used	Color	Melting point
1.	$VOSO_4.H_2O$	Dark green	280°C
2.	$CrCl_3.2H_2O$	Green	<300°C
3.	$MnSO_4.5H_2O$	Brownish red	<300°C
4.	$FeCl_3.6H_2O$	Red	288°C
5.	$CoCl_2.5H_2O$	Dark blue	295°C
6.	$NiCl_2.2H_2O$	Light red	282^0C
7.	$CuCl_2.2H_2O$	Dark green	270^0C
8.	$ZnSO_4.7H_2O$	Off-white	290^0C

B. RESULTS AND DISCUSSION

The data obtained from analytical and physico-chemical studies have been correlated to explain the properties, structure and bonding of the compounds.

1. Characterization of the ligand

The Schiff base ligand derived from *o*-hydroxyacetophenone, acetoacetanilide and 1, 2-ethylenediamine was yellow colored crystals, soluble in non-polar solvents like DMSO, benzene, etc. The homogeneity and purity of the ligand was tested by TLC technique. Melting point (185^0C) of ligand was determined using a Fisher-Johns apparatus. The ligand was characterized by elemental analysis, IR- ^{1}H NMR- and UV-Vis spectral studies.

a. Elemental analysis

The ligand was subjected to elemental analysis on a CHN-O instrument. The experimentally found and calculated percentages of C, H and N were in good agreement, confirming molecular formula of the ligand as, $C_{20}H_{23}N_3O_2$. **(Table. 2)**

Table. 2 Elemental analysis of the ligand, HEAc

Ligand	Carbon (%)		Hydrogen (%)		Nitrogen (%)	
	Found	Calculated	Found	Calculated	Found	Calculated
$C_{20}H_{23}N_3O_2$	70.59	71.19	7.09	6.89	11.98	12.45

b. ^{1}H NMR spectrum

The ^{1}H NMR spectrum of the ligand, HEAc was recorded in DMSO-d_6. The spectrum showed a number of peaks that were characteristic of the compound[33-34]. A sharp singlet at 9.20 ppm may be assigned to the -NH proton of acetoacetanilide moiety. The signals observed in the range 7.18 - 7.60 ppm may be assigned to the different aromatic protons of acetoacetanilide moiety. There was a singlet at 3.20 ppm, which may be attributed to the active methylene protons of acetoacetanilide. The signals observed in the range 6.88 – 7.49 ppm may be assigned to aromatic protons of o-hydroxyacetophenone moiety. A singlet appeared at 4.65 ppm may be attributed to the –OH proton of the *o*-hydroxyacetophenone. The triplet peak appeared at 2.68 ppm was assigned to the methylinic proton of the ethylenediimine moiety. The inductive effect of the nitrogen atoms might be responsible for the higher value. A singlet appeared at 1.95 ppm may be assigned to the protons of the $–CH_3$ group on either sides of the imine group. (**Fig. 1** & **Table. 3**)

Fig. 1: ^{1}H NMR data of the ligand, HEAc

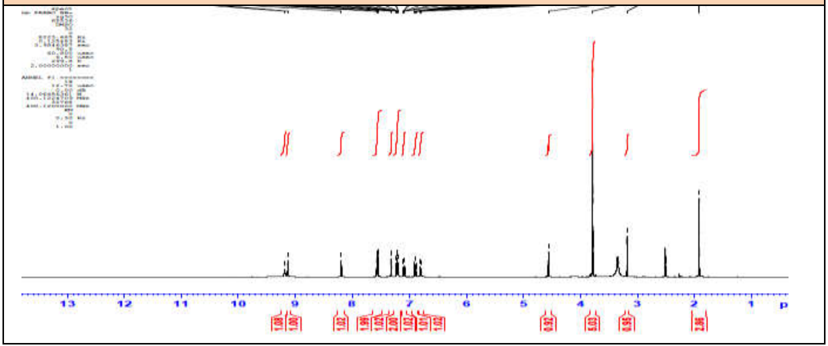


Table. 3. ^{1}H NMR data of ligand, HEAc

Si.No.	Chemical shift (ppm)	Assignment
1.	9.20 (s)*	-NH proton
2.	7.18-7.60 (m)	Aromatic protons of acetanilide
3.	6.88-7.49 (m)	Aromatic protons of *o*-hydroxyphenone
4.	3.20 (s)	$-CH_2$ active methylene protons
5.	3.67 (s)	$-CH_3$ proton
6.	4.65 (s)	-OH proton
7.	2.68 (t)	two-CH_2 proton near imine group
8.	1.95 (s)	two–CH_3 proton either side of imine group

***s= singlet, t= triplet, q= quartet**

c. IR spectrum

IR spectrum of ligand showed a medium intensity band at 3160 and a strong one at 1655 cm^{-1}, characteristic of $\nu_{\mathbf{-NH-}}$ and $\boldsymbol{\nu}_{\mathbf{-C=O}}$ of amide group (-CO-NH-), respectively. The bands present at 1633 and 1231 cm^{-1} were assigned to $\boldsymbol{\nu}_{\mathbf{-C=N}}$ and $\boldsymbol{\nu}_{\mathbf{=N-C-}}$, respectively. A band at 3063 cm^{-1} may be assigned to the aromatic $\nu_{\mathbf{=CH}}$ and another one at 2905 cm^{-1} to the $\boldsymbol{\nu}_{\mathbf{-CH}}$ of methylene group.

The bands at 2967 and 2939 cm^{-1} are due to the symmetric-and asymmetric stretching vibrations of >CH_2 group. A broad band at 3445 cm^{-1} may be assigned to the phenolic $\boldsymbol{\nu}_{\mathbf{-OH}}$ of o-hydroxyacetophenone moiety. The characteristic bands due to the stretching of >C=O in the acetoacetanilide and *o*-hydroxyacetophenone, in the range, 1648-1660 cm^{-1} were not present in the spectrum of the ligand, which indicated the complete condensation of the carbonyl compounds with 1,2-ethylinediamine. A sharp band at 1215 cm^{-1} may be assigned to the $\boldsymbol{\nu}_{\mathbf{-C\text{-}OCH3}}$ of ethoxy group. (**Table. 4 & Fig. 2**)

Fig. 2: IR spectrum of the ligand, HEAc

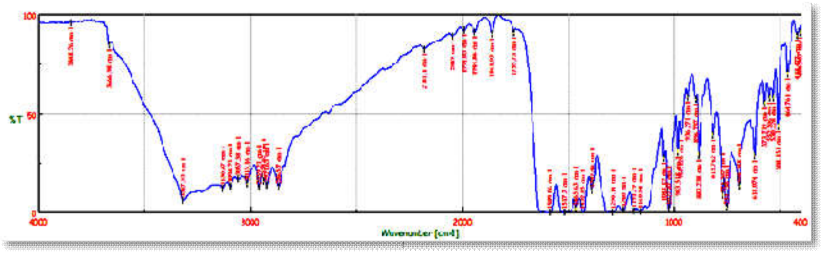


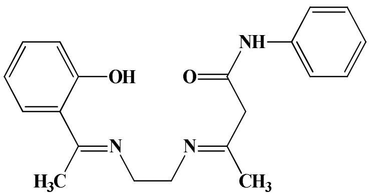
Table. 4: Significant IR bands of HEAc their assignments

Band frequency* (cm^{-1})	Assignment
3160 1665	ν_{-NH} amide $\nu_{C=O}$ amide
1633	$\nu_{>C=N}$
3063 2905	ν aromatic –CH ν_{-CH2} (Methylene)
1231	$\nu_{>C-N-}$
3445	-OH stretching vibration
1215	ν_{-CO-} (ethoxy)
874 819	out of plane bending –CH (aromatic)

d. Electronic spectrum

The UV-visible spectrum of the ligand, HEAc was recorded in DMSO at room temperature. The peak at 37,878 cm^{-1} was attributed to $\pi \rightarrow \pi^*$ transition. It may be due to the presence of aromatic part in the ligand. A peak at 24,752 cm^{-1} was due to $n \rightarrow \pi^*$ transition of the non-bonding electrons present on the oxygen of the keto (>C=O) group and nitrogen of the azomethine (>C=N) groups in the ligands[35]. From the above data, the following structure was assigned to HEAc. **(Fg. 3)**

Fig. 3: Structure of the ligand, HEAc



2. Characterization of metal complexes

a. Analytical data

All the complexes were found to be colored except that of Zn(II). They were non-hygroscopic and photo-stable. They were soluble in DMF and DMSO but only sparingly soluble in common organic solvents. The data obtained from analytical and molar conductance studies in DMF showed that the complexes have the formulae as shown in **Table.5**.

Aqua complexes were obtained for Cr(III) and Mn(II). The magnetic- and various spectral data also confirmed the suggested molecular formulae.

Table. 5: Analytical data of complexes

Empirical Formula	F^*. Wt	Elemental %, Found (Calculated)				
		M	**C**	**H**	**N**	**Anion**
$(VO)C_{20}H_{21}N_3O_3$	418.10	12.97 (12.18)	56.87 (57.42)	5.88 (5.06)	10.61 (10.04)	
$CrC_{20}H_{23}N_3O_4Cl$	440.08	12.01 (11.79)	55.01 (54.49)	5.88 (5.26)	10.01 (9.53)	8.75 (8.04)
$MnC_{20}H_{25}N_3O_5$	438.09	12.97 (12.53)	55.00 (54.80)	5.01 (4.83)	10.00 (9.59)	----
$FeC_{20}H_{23}N_3O_4Cl$	458.06	12.89 (12.17)	51.86 (52.37)	5.01 (4.61)	10.07 (9.16)	8.07 (7.73)
$CoC_{20}H_{21}N_3O_3$	410.09	15.01 (14.36)	59.01 (58.54)	4.91 (5.16)	9.98 (10.24)	---
$NiC_{20}H_{21}N_3O_3$	409.09	15.02 (14.31)	59.08 (58.58)	4.78 (5.16)	11.01 (10.25)	---
$CuC_{20}H_{21}N_3O_3$	414.09	16.01 (15.31)	56.98 (57.89)	4.85 (5.10)	10.75 (10.13)	---
$ZnC_{20}H_{25}N_3O_5$	415.09	16.01 (15.69)	56.99 (57.64)	4.99 (5.08)	10.70 (10.08)	---

b. Molar conductance data

The molar conductances at room temperature were determined using 10^{-3} M solution of the complexes in DMSO and are given in the **Table. 6**. The values were in the low range, 13-40 $\Omega^{-1}mol^{-1}cm^2$ indicating the non-electrolytic nature of the complexes and accordingly, they were assigned formulae. Analytical data and spectral studies also supported the suggested molecular formulae. (**Table. 6**)

Table. 6: Molar conductance of complexes in DMSO		
Si No:	**Complexes**	**Λ_m ($\Omega^{-1}mol^{-1}cm^2$)**
1.	**[(VOL]**	**39**
2.	**$[CrL(H_2O)Cl]$**	**35**
3.	**$[MnL(H_2O)_2]$**	**20**
4.	**$[Fe(LH_2)Cl_3]$**	**40**
5.	**[CoL]**	**34**
6.	**[NiL]**	**28**
7.	**[CuL]**	**23**
8.	**$[ZnL(H_2O)_2]$**	**14**
$L = C_{20}H_{23}N_3O_3$		

c. Magnetic moment

The magnetic susceptibilities of the complexes were measured using the Gouy balance at room temperature. $Hg[Co(NCS)_4]$ was used as the celebrant. Diamagnetic corrections were applied using Pascal constants for atoms and structural units of the complexes. The magnetic susceptibilities, diamagnetic corrections and the effective magnetic moment values were calculated. The magnetic moment values are given in the **Table.7**

In the present investigation, the VO(II) complex of HEAc showed a magnetic moment 1.71 B.M. The Cr(III) complex of HEAc showed a magnetic moment value of 3.89 B.M., which indicated its octahedral geometry. In the present case, the Mn(II) complex exhibited a magnetic moment value of 5.90 B.M. indicating its octahedral geometry. Fe(III) HEAc Schiff base complex showed a magnetic moment value at 5.89 B.M, which may be due to its to its high-spin octahedral geometry.

In the present case Co(II) showed a magnetic moment value of 4.79 B.M which may be assigned tetrahedral structure. The Ni(II) complex exhibited a magnetic moment at 3.39 B.M indicating its tetrahedral geometry. The observed magnetic moment of Cu(II) complex was 2.00 B.M. indicating its tetrahedral geometry. (**Table. 7**)

Table. 7: Magnetic moment data of complexes		
Si No:	**Complexes**	**μ_{eff} (B.M)**
1.	[(VOL]	1.71
2.	[CrL(H_2O)Cl]	3.89
3.	[MnL(H_2O)$_2$]	5.90
4.	[Fe(L)(H_2O)Cl]	5.89
5.	[CoL]	4.79
6.	[NiL]	3.39
7.	[CuL]	2.00
μ_{eff} = Effective magnetic moment, B.M = Bohr Magneton		

d. Electronic spectra

The electronic spectrum of [VOL] exhibited bands at 13,350, 19,400 and 24,200 cm^{-1}, which are assignable to transitions, $^2B_2 \rightarrow {}^2E$ (ν_1), $^2B_2 \rightarrow {}^2B_1$ (ν_2), and $^2B_2 \rightarrow {}^2A_1$ (ν_3), respectively. The geometry of this complex can be assigned as tetragonal pyramidal[52]. The value of the magnetic moment for this complex was 1.71 B.M., which indicated the presence of one unpaired electron in it[36].

In the spectrum of the Cr(III) complex investigated here two band observed at 16,800 and 22,300 cm^{-1} were assigned, respectively, to $^4A_{2g} \rightarrow {}^4T_1$ and the $^4A_{2g} \rightarrow {}^4T_{2g}$ transitions characteristics of an octahedral Cr(III) complex. Octahedral environment of Cr(III) complex, exhibited a third transition corresponding $^4A_{2g} \rightarrow {}^4T_{1g}$ (P) above 30400 cm^{-1} but in this region the $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ intraligand bands are also observed[37-39]. Magnetic moment data also supported its octahedral geometry.

The brown coloured [MnL(H_2O)$_2$] exhibited bands at 14,100 cm^{-1}, 20,400 cm^{-1} and 24,200 cm^{-1}. They may be assigned to $^6A_{1g} \rightarrow {}^4T_{1g}$, $^6A_{1g} \rightarrow {}^4T_{2g}$ and $^6A_{1g} \rightarrow {}^4E_g$ transitions of an octahedral Mn(II) complex[39].

In the present investigation, the Fe(III) complex was found to be red and it registered two bands, one at 25,000 and another broad one at 20,000 cm^{-1} and were assigned to d-d transitions in an octahedral field[40,41]. Its magnetic moment value, 5.89 B.M supported the geometry.

In the present investigation, the spectrum of Co(II) HEAc complex showed bands at 7640, 8750 and 15900 cm^{-1} and were assigned, respectively to the $^4A_2 \rightarrow ^4T_2$ (ν_1), $^4A_2 \rightarrow ^4T_1$ (ν_2) and $^4A_2 \rightarrow ^4T_1$ (P) (ν_3)[42] transitions of a tetrahedral Co(II) complex. The deep blue color of the complex and its magnetic moment data supported this structure.

The Ni(II) complex investigated here exhibited three transitions characteristic of tetrahedral geometry. Bands were identified at 7,340, 8,100 and 14,300 cm^{-1} and were assigned to $^3T_1 \rightarrow$ $^3T_2$, $^3T_1 \rightarrow ^3A_2$ and $^3T_1 \rightarrow ^3T_1(P)$,[42] respectively.

The 4- coordinate Cu(II) belongs to the d^9 system. In the present case, the spectrum of Cu(II) HEAc complex showed an intense transition at 23,700 cm^{-1} and was assigned to the $^2T_2 \rightarrow ^2E$ transition, which indicated its tetrahedral geometry[42]. (**Table. 8**)

Table. 8: Electronic spectra of complexes and their assignments

Si. No:	Complexes	Bands (cm^{-1})	Assignments	Geometry
1.	[(VOL]	13,350	$^2B_2 \rightarrow ^2E$	Tetragonal Pyramid
		19,400	$^2B_2 \rightarrow ^2B_1$	
		24,200	$^2B_2 \rightarrow ^2A_1$	
2.	[CrL(H_2O)Cl]	16,800	$^4A_{2g} \rightarrow ^4T_1$	Octahedral
		22,300	$^4A_{2g} \rightarrow ^4T_{2g}$	
3.	[MnL(H_2O)$_2$]	14,100	$^6A_{1g} \rightarrow ^4T_{1g}$	Octahedral
		20,400	$^6A_{1g} \rightarrow ^4T_{2g}$	
		24,200	$^6A_{1g} \rightarrow ^4E_g$	
4.	[Fe(LH_2)Cl_3]	20,870	$^6A_{1g} \rightarrow ^4T_{2g}$	Octahedral
		24,200	CT	
5.	[CoL]	7,640	$^4A_2 \rightarrow ^4T_2$	Tetrahedral
		8,750	$^4A_2 \rightarrow ^4T_1$	
		15,900	$^4A_2 \rightarrow ^4T_1(P)$	
6.	[NiL]	7,340	$^3T_1 \rightarrow ^3T_2$	Tetrahedral
		8,100	$^3T_1 \rightarrow ^3T_2$	
		14,300	$^3T_1 \rightarrow ^3T_1(P)$	
7.	[CuL]	23,700	$^2T_2 \rightarrow ^2E$	Tetrahedral

e. IR spectra

As a versatile technique for structure and chemical studies, the IR spectroscopy is extremely helpful for the identification and characterization of compounds and in assigning geometries to them. The significant vibrational bands of the HEAc metal complexes and the assignments are given in **Table. 9**.

The IR spectrum of the ligand showed a medium intensity band at 3100 and a strong one at 1655 cm^{-1}, respectively, due to ν_{-NH-} and $\nu_{-C=O}$ of amide group (-CO-NH-). The bands at 1655 cm^{-1} was absent in the spectra of all the complexes. This indicated that the –NH-CO-CH_2- (amide group) of acetoacetanilide moiety has undergone enolisation to –CH=C-OH and after deprotonation coordinated to the metal ion. This was supported by the appearance of new bands around 1115 cm^{-1} due to ν_{-C-O} in the spectra of the complexes.

Band of medium intensity at 1633 cm^{-1} in the spectrum of ligand may be assigned to $\nu_{-C=N}$. However, the spectra of all the complexes, this band shifted to a lower frequency region by 5 to 10 cm^{-1}, indicating participation of azomethine nitrogens in coordination.

The IR spectrum of ligand showed a medium intensity band at 3015 and a strong band at 1655 cm^{-1} due to characteristic ν_{-NH-} and $\nu_{-C=O}$ of amide group (-CO-NH-), respectively. However the bands at 1633 cm^{-1} were absent in the spectra of all the complexes. Such a situation indicted that the amide group changed in the complexes, that means, the -C=O group of –NH-CO- (amide group) participated in complexation, through the enolization of –CH_2-C=O to –CH=C-OH and subsequent coordination through the deprotonated oxygen. The above fact supported by the appearance of new bands around 1145 cm^{-1} due to ν_{-C-O} in the spectra of the complexes.

The band at 3063 cm^{-1} may be assigned to the aromatic ν_{-CH} and that at 2905 cm^{-1} to the ν_{-CH} of the methylene group. A characteristic non-ligand sharp band in the spectrum of VO(II) complex at 961 cm^{-1} has been assigned to $\nu_{V=O}$[43].

Broad bands at ~ 3500-3460 cm^{-1} in the spectra of the complexes of Cr(III), Mn(II), Fe(III) and Zn(II) were attributed to the hydroxyl stretching modes of water molecules. In addition, strong bands ~ 870-980 and ~ 650 cm^{-1} suggested that the water molecules were coordinated.[44] Medium bands around 510-540 cm^{-1} and 415-450 cm^{-1} in the spectra all the complexes may be assigned[45] to ν_{M-N} and ν_{M-O}, respectively. Bands at 400 and 410 cm^{-1} in the spectra of Cr(III) and Fe(III) complex indicated the presence of M-Cl bond in these complexes. (**Table.9 & Fig. 4-7**)

Table. 9: Significant bands in the IR spectra and their assignments

	Assignments and band frequencies (cm^{-1})						
Compounds	$\nu_{-C=N}$	ν-amide	ν_{-OH} (H_2O)	$\nu_{N=C-O}$ (enolised)	ν_{-M-N}	ν_{-M-O}	ν_{-M-Cl}
VEAc (LH_2)	1633	3015, 1655	3445	-----	-----	---	----
[(VOL]	1620	3012 ---	----	1130, 1044	515	480	----
[$CrL(H_2O)Cl$]	1618	3017 ---	3405	1120, 1030	520	470	414
[$MnL(H_2O)_2$]	1620	3018 ---	3410	1120, 1019	523	474	---
[$FeL(H_2O)Cl$]	1615	3014 ---	3595	1140, 1030	515	469	410
[CoL]	1619	3014 ----	-----	1124, 1071	519	480	----
[NiL]	1621	3016 ----	----	1115, 1080	515	484	---
[CuL]	1620	3014 ----	----	1120, 1038	523	470	----
[$ZnL(H_2O)_2$]	1617	3013 ----	3440	1120, 1025	518	484	----

Fig. 4: IR spectrum of VO(II) complex

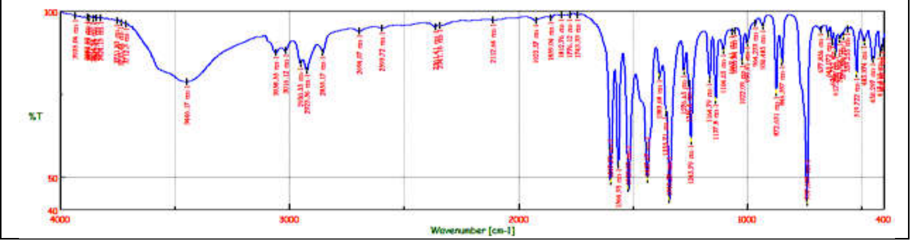


Fig. 5: IR spectrum of Co(II) complex

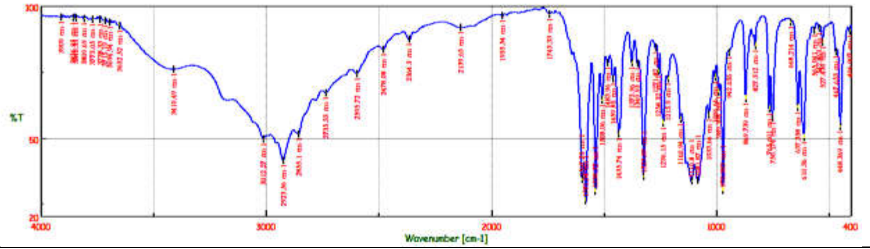


Fig. 6: IR spectrum of Ni(II) complex

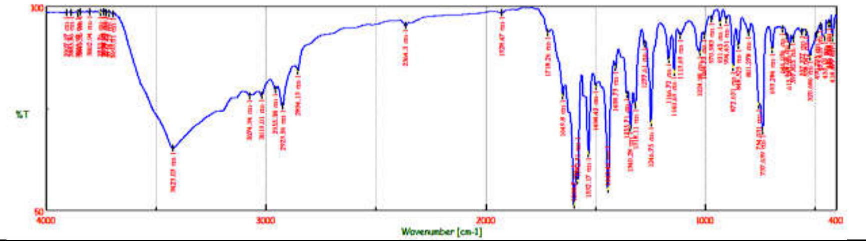
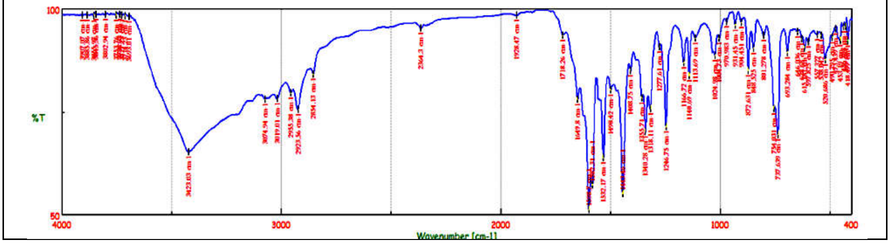


Fig. 7: IR spectrum of Zn(II) complex



On the basis of above observations, the probable structures of the HEAc Schiff base and its complexes of VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) are shown below. (**Fig. 8-13**)

Fig. 8: Structure of ligand, HEAc	**Fig. 9: Structure of [VOL]**

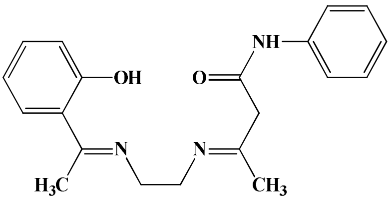
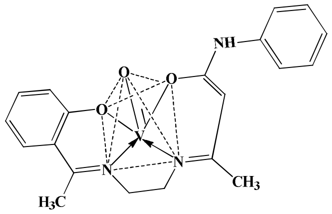

	

Fig. 10: Structure of [CrL(H_2O)Cl]	**Fig. 11: Structure of [FeL(H_2O)Cl]**

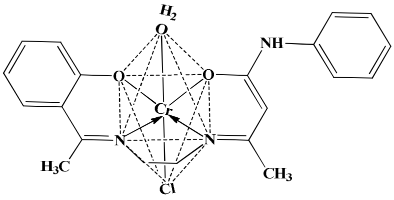
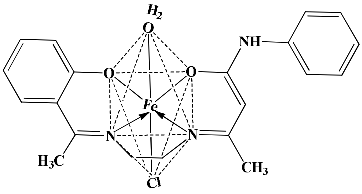
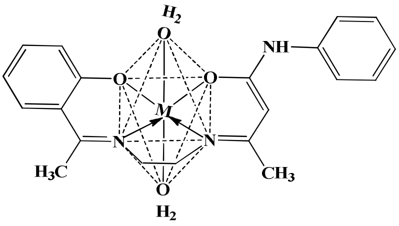
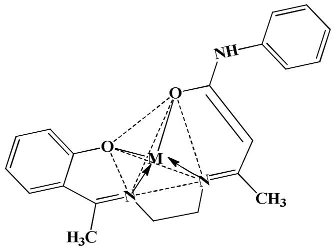

	

Fig. 12: Structure of [ML(H_2O)$_2$], where M = Mn(II) and Zn(II)	**Fig. 13: Structure of [ML], where M = Co(II), Ni(II) and Cu(II)**
	

C. CONCLUSIONS

Novel Schiff base ligand, *o*-hydroxyacetophenone-(1,2-ethylenediimine)acetoacetanilide (VEAc) and its VO(II), Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) complexes were synthesized. The Schiff base synthesized here acted as a tetradentate ONNO donor ligand. The properties and structures of the ligand and the complexes were determined by the elemental and spectral analysis. The complexes have the general formulae, [(VO)L],

$[CrL(H_2O)Cl]$, $[MnL(H_2O)_2]$, $[FeL(H_2O)Cl]$, [CoL], [NiL], [CuL] and $[ZnL(H_2O)_2]$. Based on the analytical, magnetic and various spectral studies, geometries have been assigned to these complexes. [(VO)L] complex was found to be tetragonal pyramid, $[CrL(H_2O)Cl]$, $[MnL(H_2O)_2]$, $[FeL(H_2O)Cl]$ and $[ZnL(H_2O)_2]$ complexes were found to be octahedral and [CouL], [NiL] and [CuL] complexes were tetrahedral.

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Chapter VII

SYNTHESIS AND CHARECTERISATION OF SCHIFF BASE COMPLEXES DERIVED FROM O-HYDROXYACETOPHENONE AND ETHYLACETOACETATE WITH 1, 2-ETHYLENEDIAMINE

Schiff bases, an important class of organic ligands are formed by the condensation of carbonyl compounds and primary amines[1]. Nowadays, they are treated as a "privileged ligands" due to the ease of preparation, capability to coordinate to various metals ions and to stabilize the metal ion in different oxidation states thereby controlling the activity of metals in various catalytic reactions due to the potential ability of such compounds to act as chelating ligands by binding through imine nitrogen and another atom such as oxygen or sulphur, etc., they have a significant in the field of inorganic coordination chemistry.

Schiff bases ligands and their metal complexes have a large variety of applications in several fields, including pharmaceutical-, medicinal-, analytical-, agriculture- and industrial fields[2,3]. They are used as catalysts in both homogeneous and heterogeneous reactions, intermediates in organic synthesis, polymer additives, synthetic dyes, ion-exchange chromatographic resins, and anticorrosion agents. Besides their industrial uses, Schiff bases also show a wide range of potential biological activities such as antimalarial-, antibacterial-, antifungal-, cytotoxic and anticancer activities. The bioassay of Schiff bases have been well reported in recent times[4].

A search through the literature revealed that no work has been done on the transition metal complexes of the Schiff base derived from *o*-

hydroxyacetophenone, ethylacetoacetate and 1,2-ethylenediamine. In this chapter we report the synthesis and characterization of a new type of dianionic-bidentate/tetradentate ligand formed by the condensation of *o*-hydroxyacetophenone and ethylacetoacetate with 1,2-ethylenediamine and its complexes with Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II). The choice of the carbonyl compounds for the preparation of this Schiff base ligand was made due to their potential biological activities[5,6].

A. Experimental

1. Materials and methods

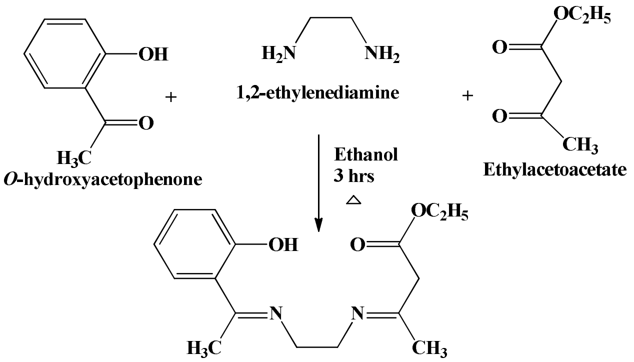
Specifications regarding the reagents used, the procedural details adopted for synthesis and characterization of the ligand and the complexes are given in the Chapter II. For the preparation of the ligand, *o*-hydroxyacetophenone, ethylacetoacetate and 1, 2-ethylenediamine was used. The metal salts used in this study were of BDH AnalaR quality. Mainly, chlorides and sulphates of Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) were used for the synthesis of the complexes.

2. Synthesis

a. *o*-hydroxyacetophenone-(1,2-ethylenediimine)ethylacetoacetate (HEE)

O-hydroxyacetophenone (0.025 mol) and ethylacetoacetate (0.025 mol) in minimum amount of ethanol were added to 1,2-ethylenediamine (0.025 mol) in ethanol in a 250 ml round bottom flask. Added a few drops of mineral acid as dehydrating agent. The mixture was refluxed for 2 h. Completion of the reaction was monitored by thin-layer chromatography (TLC) on pre-coated silica gel F_{254} plates from Merck. After the completion of the reaction, the mixture was cooled in ice bath till the yellow crystals separated. The product was filtered off, washed with ethanol and dried over anhydrous calcium chloride. (**Scheme.1**)

Scheme.1: Preparation of the ligand *o*-hydroxyacetophenone-(1,2-ethylenediimine)ethylacetoacetate (HEE)



***The systematic name of the compound is: (E)-ethyl-3-((2-((E)-(2-hydroxybenzylidene)amino)ethyl)imino)butanoate. But for the sake of convenience the name 'Ortho-hydroxyacetophenone-(1, 2-ethylenediimine)ethylacetoacetate" and the short form 'HEE' are adopted in this thesis.**

b. Complexes

Ethanolic solution of the metal salt (0.005 mol in 25 ml ethanol) was added to a solution of the ligand (0.005 mol in 25 ml in DMSO) and the mixture was refluxed for about 4 h. It was then cooled and allowed to evaporate the solvent to reduce approximately half of the total volume. The solid complexes formed were filtered off, washed several times with petroleum benzene and finally with methanol and were dried over anhydrous calcium chloride. (**Table.1**)

Table.1: Physical properties of the complexes

Si. No	Metal Salt Used	Color	Melting point
1.	$CrCl_3.2H_2O$	Green	291°C
2.	$MnSO_4.5H_2O$	Reddish-brown	290°C
3.	$FeCl_3.6H_2O$	Red	286°C
4.	$CoCl_2.5H_2O$	Dark brown	294°C
5.	$NiCl_2.2H_2O$	Dark green	298^{0}C
6.	$CuCl_2.2H_2O$	Greenish brown	285^{0}C
7.	$ZnSO_4.7H_2O$	Off-white	271^{0}C

B. RESULTS AND DISCUSSION

The data obtained from the analytical-and physico-chemical studies have been correlated to explain the properties, structure and bonding of the compounds.

1. Characterization of the ligand

The Schiff base ligand, HEE derived from *o*-hydroxyacetophenone, ethylacetoacetate and 1,2-ethylenediamine was yellow colored crystals, soluble in non-polar solvents like DMSO, DMF, benzene, etc. The homogeneity and purity of the ligand were tested by TLC technique. Melting point was determined using a Fisher-Johns apparatus. The ligand was found to melt at 184^0C. The ligand was characterized by elemental analysis, IR, ^{1}H NMR and UV-Vis spectral studies.

a. Elemental analysis

The ligand was subjected to elemental analysis on a CHN-O instrument. The experimentally found and calculated percentages of C, H and N were in good agreement, confirming its molecular formula as $C_{15}H_{20}N_2O_3$. (**Table. 2**)

Table. 2: Elemental analysis of the ligand, HEE

Ligand	Carbon (%)		Hydrogen (%)		Nitrogen (%)	
	Found	Calculated	Found	Calculated	Found	Calculated
$C_{20}H_{23}N_3O_3$	66.00	65.20	6.90	7.30	11.00	10.14

b. ^{1}H NMR spectrum

The ^{1}H NMR spectrum of the ligand, HEE was recorded in DMSO-d_6. The spectrum showed a number of peaks that were characteristic of the compound[7,8]. The signals observed in the range 7.01-7.61 ppm may be assigned to the different types of aromatic protons of the *o*-hydroxyacetophenone moiety. A singlet observed at 4.56 ppm may be assigned to –OH proton. There was a singlet at 3.26 ppm, which may be attributed to the active methylene protons of ethylacetoacetate moiety. There weas a intense triplet at 2.65 ppm, respectively due to the =N-CH_2- protons of o-hydroxyacetophenone and ethylacetoacetate moieties of the ligand HEE. The quartet appeared at 4.13 ppm and a triplet at 1.80 ppm was due to protons of –CH_2- and –CH_3 of -OC_2H_5, respectively. The singlet observed at 1.90 was due to the –CH_3 proton near azomethine group of the ligand, HEE. (**Fig. 1** & **Table.3**)

Table. 1: ^{1}H NMR spectrum of ligand, HEE

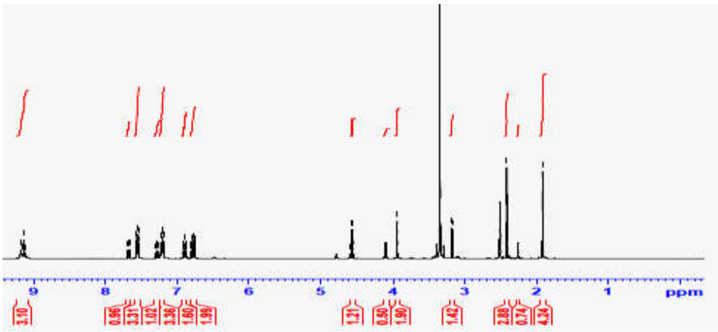


Table. 3: ^{1}H NMR data of ligand, HEE		
Sl.No.	**Chemical shift (ppm)**	**Assignment**
1.	**7.01-7.61 (m)**	**Aromatic protons**
2.	**4.13(q), 1.80(t)**	**-OC_2H_5 protons**
3.	**3.26 (s)**	**Active methylene –CH_2 proton**
4.	**4.56 (s)**	**-OH proton**
5.	**1.90 (s)**	**-CH_3 protons near imine group**
6.	**2.65 (t)**	**2 -CH_2 protons of imine**
***s= singlet, t= triplet, q= quartet**		

c. IR spectrum

The infrared spectrum of the Schiff base ligand, HEE showed a number of absorption bands, which were characteristics of various functional groups, present in it. Assignments were given on the basis of spectra of compounds of similar structures known earlier[9,10]. The assignments are given in the **Table. 4**.

The IR spectrum of ligand showed a strong band at 1630 is due to $\nu_{>C=O}$. The bands present at 1631 and 1280 cm^{-1} were assigned to the $\nu_{-C=N}$ and $\nu_{=N-C-}$, respectively. The band at 3150 cm^{-1} may be assigned to the aromatic ν_{-CH} of phenyl group. The band at 2967 and 2939 cm^{-1} were due to the symmetric-and asymmetric stretching vibrations of -CH_2 group.

A band at 3317 cm^{-1} is due to ν_{-OH} of *o*-hydroxyacetophenone moiety. The characteristic bands due to the stretching of >C=O in the *o*-hydroxyacetophenone and ethylacetoacetate, in the range 1640-1658 cm^{-1} were not present in the spectrum of the ligand, which indicated the complete condensation of the carbonyl compounds and 1,2-diamine. A sharp band at 1244 cm^{-1} may be due to the $\nu_{-O\text{-}C\text{-}}$ of ethoxy group. (**Table. 4 & Fig. 2**)

Fig. 2: IR spectrum of the ligand, HEE

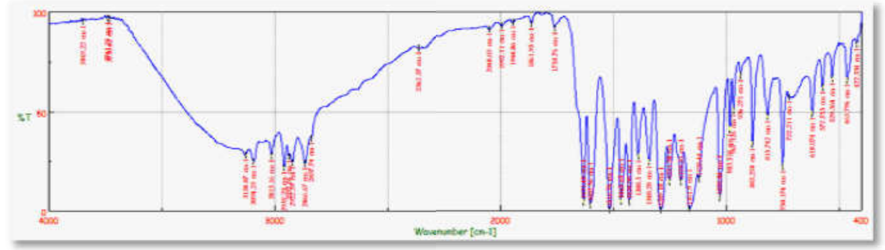


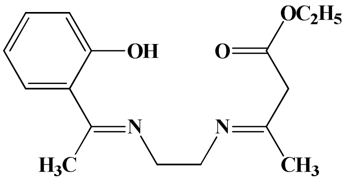
Table. 4: Significant IR bands of ligand, HEE and their assignments	
Band frequency* (cm^{-1})	**Assignment**
1631	**$\nu_{>C=N-}$ of o-hydroxyacetophenone**
1280	**$\nu_{=N\text{-}C\text{-}}$**
1630	**$\nu_{>C=O}$**
3150 **2967**	**ν aromatic –CH** **ν_{-CH2} (Methylene)**
3317	**ν_{-OH}**
1610, 1555	**δ in plane –CH (aromatic)**
1244, 1055	**ν_{-CO-} (ethoxy)**
864 **810**	**δ out of plane –CH (aromatic)**

d. Electronic spectrum

The electronic spectrum of the ligand was recorded in DMSO. The peak at 35,460 cm^{-1} was attributed to $\pi \rightarrow \pi^*$ transition. It may be due to the presence of aromatic part of the ligand. A peak at 24875 cm^{-1} may be due to the $n \rightarrow \pi^*$ transition of the non-bonding electrons present on the oxygen of the keto

(>C=O) groups and nitrogen of the azomethine (C=N) groups in the ligand[11]. From the above data, the following structure was assigned to HEE (LH_2). **(Fig. 3)**

Fig. 1 Structure of the ligand, HEE (LH_2)



2. Characterization of metal complexes

a. Analytical data

All the complexes were found to be colored [except that of Zn(II)], non-hygroscopic and photo-stable. They were soluble in DMF, DMSO, benzene, etc. but only sparingly soluble in common organic solvents. The data obtained from analytical and molar conductance studies in DMF showed that the complexes have the molecular formulae as shown in the **Table. 5**.

Aqua complexes were obtained for Cr(III), Mn(II), Fe(III), Co(II), Ni(II) and Cu(II). Magnetic susceptibility and various spectral data also confirmed the suggested molecular formulae of the complexes. (**Table. 5**)

Table. 5: Analytical data of complexes

Compound	F^*. Wt	Elemental %, Found (Calculated)				
		Metal	C	H	N	Anion
$[CrL(H_2O)Cl]$	379	13.00 (13.69)	46.55 (47.44)	6.04 (5.31)	8.01 (7.38)	8.84 (9.34)
$[MnL(H_2O)_2]$	365	14.61 (15.04)	51.00 (49.32)	5.95 (6.07)	8.01 (7.67)	----
$[FeL(H_2O)Cl]$	383	13.79 (14.56)	47.86 (46.96)	5.00 (5.25)	6.77 (7.30)	10.01 (9.24)
$[CoL(H_2O)_2]$	369	16.02 (15.96)	49.00 (48.79)	5.75 (6.00)	8.06 (7.59)	---
$[NiL(H_2O)_2]$	369	16.22 (15.90)	47.95 (48.82)	5.69 (6.01)	6.88 (7.59)	---
$[CuL(H_2O)_2]$	373	16.78 (17.00)	49.47 (48.19)	6.31 (5.93)	8.05 (7.49)	---
[ZnL]	339	18.68 (19.25)	52.99 (53.04)	4.97 (5.34)	9.05 (8.25)	---

b. Molar conductance

The molar conductances at room temperature were determined using 10^{-3} M solutions of the complexes in DMSO and are given in the **Table. 6**. The molar conductance values were in the range 13 -32 μ ohm/cm, indicating the non-electrolytic nature of the complexes and accordingly, they were assigned formulae. Analytical data and spectral studies also supported the suggested formulae.

Table. 6: Molar conductance of complexes in DMSO

Si No:	Complexes	Λ_m ($\Omega^{-1}mol^{-1}cm^2$)
1.	$[CrL(H_2O)Cl]$	29
2.	$[MnL(H_2O)_2]$	14
3.	$[Fe(LH_2)Cl_3]$	18
4.	$[CoL(H_2O)_2]$	21
5.	$[NiL(H_2O)_2]$	32
6.	$[CuL(H_2O)_2]$	20
7.	[ZnL]	16
L = $C_{17}H_{23}N_3O_3$		

c. Magnetic moment data

The magnetic susceptibility of the complexes was measured using a Gouy balance at room temperature. Hg[Co(NCS)$_4$] was used as the calibarant. Diamagnetic corrections were applied using Pascal constants for atoms and structural units of the complexes. The magnetic susceptibilities, diamagnetic corrections and the effective magnetic moment values were calculated. The corrected magnetic susceptibilities are given in the **Table. 7**

The HEE Schiff base complex of Cr(III) showed a magnetic moment value of 3.84 B.M., which indicated its octahedral geometry. In the present case [MnL(H$_2$O)$_2$] complex showed a value of 5.81 B.M indicating its octahedral geometry[12-14]. [FeL(H$_2$O)(Cl)] complex registered a magnetic moment value of 5.80 B.M. which may be due to its octahedral geometry.

[CoL(H$_2$O)$_2$] registered a magnetic moment of 5.19 B.M. The value indicated its octahedral geometry. The HEE Schiff base complex of Ni(II) and Cu(II) investigated here registered a magnetic moment values of 3.35 and 1.90 B.M., respectively, indicating their octahedral geometry.

Table. 7: Magnetic moment data of complexes

Si No.	Complexes	μ_{eff} (B.M)
1.	[CrL(H$_2$O)Cl]	3.84
2.	[MnL(H$_2$O)$_2$]	5.81
3.	[Fe(L)(H$_2$O)Cl]	5.80
4.	[CoL(H$_2$O)$_2$]	5.19
5.	[NiL(H$_2$O)$_2$]	3.35
6.	[CuL(H$_2$O)$_2$]	1.90

μ_{eff} = Effective magnetic moment, B.M = Bohr magneton

d. Electronic spectra

In the electronic spectrum of the Cr(III) complex investigated here two bands were observed at 16,880 and 22,400 cm^{-1} and were assigned, respectively, to the $^4A_{2g}\rightarrow {}^4T_1$ (P) and the $^4A_{2g}\rightarrow {}^4T_{2g}$ transition characteristics of an octahedral geometry[15-17].

The spectrum of the Mn(II) complexes exhibited a number weak bands in the region, 16,000 - 25,100 cm^{-1} which are assigned to d-d transitions in an octahedral field. The brown coloured $[MnL(H_2O)_2]$ exhibited some electronic transitions at 14,400 cm^{-1}, 20,100 cm^{-1} and 24,700 cm^{-1} and were assigned to the $^6A_{1g}\rightarrow {}^4T_{1g}$, $^6A_{1g}\rightarrow {}^4T_{2g}$ and $^6A_{1g}\rightarrow {}^4E_g$ transitions characteristic of octahedral geometry[17].

Most of the electronic transitions of Fe(II) are at very high energy region and they give no information about the type of bands responsible from them. In the present investigation, the $[Fe(L)(H_2O)Cl]$ was found to be pale red and gave only weak bands in the range 24,900 – 20,500 cm^{-1}. These were assigned to d-d transitions of Fe(III) ion in an octahedral field[18,19].

The spectrum of Co(II) HEE complex showed bands at 9852, 16,077 and 20,920 cm^{-1} and were assigned, respectively, to $^4T_{1g}\rightarrow {}^4T_{2g}$ (ν_1), $^4T_{1g}\rightarrow {}^4A_{2g}$ (ν_2) and $^4T_{1g}\rightarrow {}^4T_{1g}$(P) ($\nu_3$) transitions of an octahedral Co(II) complex[20].

The Ni(II) complex investigated here exhibited three transitions corresponding to octahedral geometry. Bands were identified at 8710, 14084 and 25706 cm^{-1} and were assigned, respectively, to $^3A_{2g}\rightarrow {}^3T_{2g}$, $^3A_{2g}\rightarrow {}^3T_{1g}$ and $^3A_{2g}\rightarrow {}^3T_{1g}$(P)[20] transitions The ratio of wave numbers of the transition assigned as $^3A_{2g}\rightarrow {}^3T_{2g}$ (F) and $^3A_{2g}\rightarrow {}^3T_{1g}$(F) was found to be 1.6 confirming octahedral geometry of the complex..

The six coordinate Cu(II) complexes belong to d^9 system. A single absorption band representing the $^2E_{2g}\rightarrow {}^2T_{2g}$ transition is observed in the octahedral geometry. In the present case, the spectrum of Cu(II) HEE complex exhibited an intense transition at 14,409 cm^{-1} and was assigned to the $^2E_{2g}\rightarrow {}^2T_{2g}$ transition indicating the octahedral geometry[20]. (**Table. 8**)

Table. 8: Electronic spectra of HEE complexes

Si. No:	Complexes	Bands (cm^{-1})	Assignments	Geometry
1.	$[CrL(H_2O)Cl]$	16,880	$^4A_{2g}\rightarrow{}^4T_1$ (P)	Octahedral
		22,400	$^4A_{2g}\rightarrow{}^4T_{2g}$	
2.	$[MnL(H_2O)_2]$	14,400	$^6A_{1g}\rightarrow{}^4T_{1g}$	Octahedral
		20,100	$^6A_{1g}\rightarrow{}^4T_{2g}$	
		24,700	$^6A_{1g}\rightarrow{}^4E_g$	
3.	$[Fe(LH_2)Cl_3]$	19,920	$^6A_{1g}\rightarrow{}^4T_{2g}$	Octahedral
		24,100	CT	
4.	$[CoL(H_2O)_2]$	9,852	$^4T_{1g}\rightarrow{}^4T_{2g}$	Octahedral
		16,077	$^4T_{1g}\rightarrow{}^4A_{2g}$	
		20,920	$^4T_{1g}\rightarrow{}^4T_1(P)$	
5.	$[NiL(H_2O)_2]$	8,710	$^3A_{2g}\rightarrow{}^3T_{2g}$	Octahedral
		14,084	$^3A_{2g}\rightarrow{}^3T_{1g}$	
		25,706	$^3A_{2g}\rightarrow{}^3T_1(P)$	
6.	$[CuL(H_2O)_2]$	14,409 b	$^2E_g\rightarrow{}^2T_{2g}$	Octahedral

e. IR spectra

An IR spectral technique is exceptionally useful for the identification and characterization of metal complexes and in assigning their structures and bonding. The probable assignments are given in **Table. 9**.

Band of medium intensity at 1631 cm^{-1} in the spectrum of ligand may be assigned to $\nu_{C=N}$. However, in the spectra of all the complexes, this band was found to be shifted to a lower frequency region by a few cm^{-1}, indicating the coordination of azomethine nitrogen with metal ions.

Disappearance of $\nu_{-C=O}$ band (1630 cm^{-1}) in the spectra of all the complexes indicated that the chelation took place through the enolic ν_{-OH} by after deprotonation. The new bands observed around 1124 cm^{-1}, confirmed the enolisation of $–CH_2\text{-}C=O$ to $–CH=C\text{-}OH$ and subsequent coordination through the deprotonated oxygen (O^-).

The band at 3063 cm^{-1} may be assigned to the aromatic –CH stretching and that at 2905 cm^{-1} due to the ν_{-CH} of the methylene group. Sharp bands at 1210 and 1050 cm^{-1} were due to $\nu_{C\text{-}O}$ of ethoxy group. Broad bands ~ 3500-3460 cm^{-1}

in the spectra of Cr(III), Mn(II), Fe(III), Co(II), Ni(II) and Cu(II) complexes were attributed to the hydroxyl stretching modes of water molecules. In addition, the strong bands ~ 870-980 and ~ 650 cm^{-1} suggested the coordinated nature of water molecules[21].

Medium bands in the ranges 510-550 and 415-440 cm^{-1} in the spectra of all the complexes may be assigned to **$\nu_{(M-N-)}$** and **$\nu_{(M-O-)}$**, respectively[22]. Bands in the range 415-425 cm^{-1} in the spectra of Cr(III) and Fe(III) complex indicated in the presence of M-Cl bonds. (**Table. 9 & Fig. 4-8**)

Fig. 4: IR spectrum of Cr(III) complex

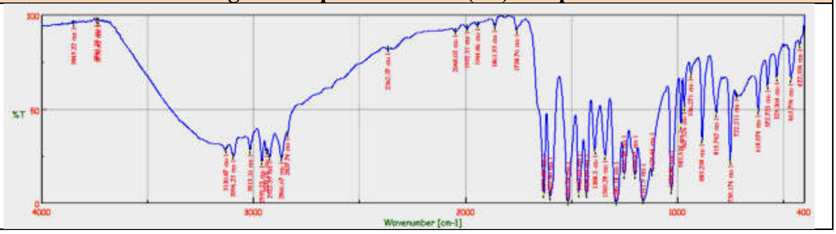


Table. 9 Significant IR bands of HEE and its complexes and their assignments

Compounds	Assignments and band frequencies (cm^{-1})						
	$\nu_{-C=N}$	$\nu_{-C=O}$	ν_{-OH} (H_2O)	$\nu_{=C-O}$ (enolised)	ν_{-M-N}	ν_{-M-O}	ν_{-M-Cl}
HEE (LH_2)	1631	1630	3317	----	-----	---	----
[$CrL(H_2O)Cl$]	1620	--	3441	1120, 1030	520	460	413
[$MnL(H_2O)_2$]	1621	--	3420	1125, 1023	527	476	---
[$FeL(H_2O)Cl$]	1620	--	3500	1140, 1030	523	480	413
[$CoL(H_2O)_2$]	1621	--	3348	1150, 1070	510	490	----
[$NiL(H_2O)_2$]	1618	--	3390	1150, 1098	510	466	---
[$CuL(H_2O)_2$]	1619	--	3405	1140, 1026	521	475	----
[ZnL]	1620	--	-----	1150, 1020	533	469	----

Fig. 5: IR spectrum of Co(II) complex

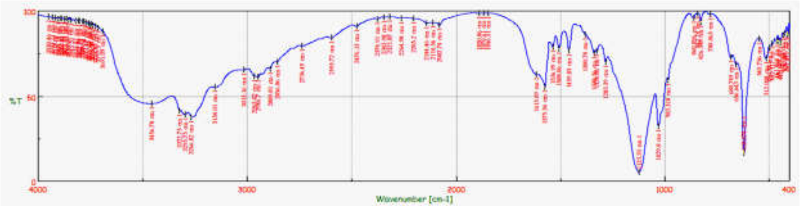


Fig. 6: IR spectrum of Ni(II) complex

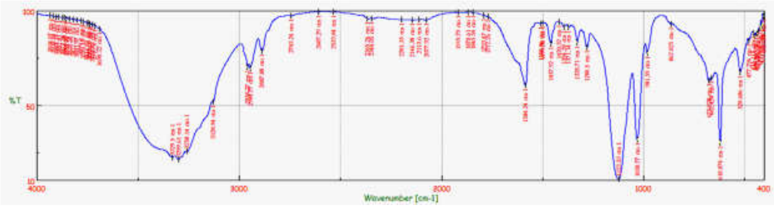


Fig. 7: IR spectrum of Cu(II) complex

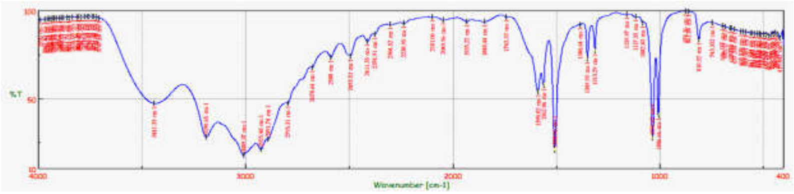
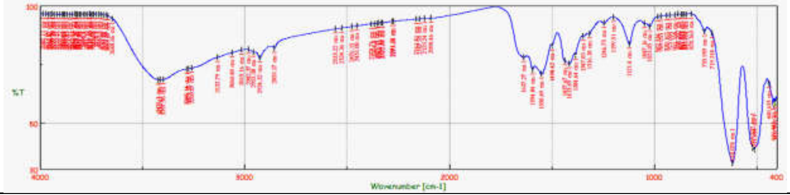


Fig. 8: IR spectrum of Zn(II) complex



On the basis of above observations, the probable structures of the HEE Schiff base ligand and its complexes of Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) are shown below (**Fig. 9-12)**

Fig.9: Structure of the ligand, HEE

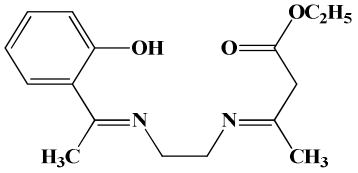


Fig. 10: Structure of $[ML(H_2O)Cl]$, where M = Cr(III) and Fe(III)

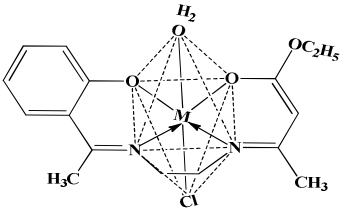


Fig. 11: Structure of $[ML(H_2O)_2]$, where M = Mn(II), Co(II), Ni(II) and Cu(II)

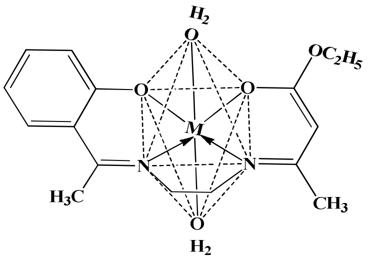
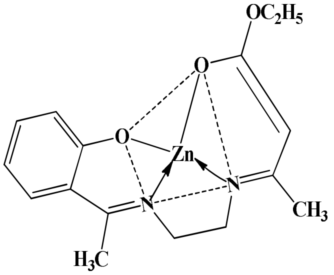


Fig. 12: Structure of [ZnL]



C. CONCLUSIONS

Coordination complexes of Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) were synthesized with a multidentate ONNO donor Schiff base ligand, o-hydroxyacetophenone-(1,2-ethylenediimine)ethylacetoacetate (L2H) and their physico-chemical properties have been studied. The ligand, o-hydroxyacetophenone-(1,2-ethylenediimine)ethylacetoacetate (HEE) was synthesized by condensing of *o*-hydroxyacetophenone, ethylacetoacetate and 1,2-ethylenediamine in 1:1:1 molar ratio. The complexes have the general formulae, $[CrL(H_2O)Cl]$, $[MnL(H_2O)_2]$, $[FeL(H_2O)Cl]$, $[CoL(H_2O)_2]$, $[NiL(H_2O)_2]$, $[CuL(H_2O)_2]$ and [ZL] Based on the analytical-, magnetic- and various spectral studies, geometries have been assigned to these complexes. $[CrL(H_2O)Cl]$, $[MnL(H_2O)_2]$, $[FeL(H_2O)Cl]$, $[CoL(H_2O)_2]$, $[NiL(H_2O)_2]$ and $[CuL(H_2O)_2]$ complexes were found to be octahedral and [ZL] complexe was found to be tetrahedral in geometry.

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Chapter VIII

SYNTHESIS AND CHARECTERISATION OF SCHIFF BASE COMPLEXES DERIVED FROM *O*-VANILLIN AND *O*-HYDROXYACETOPHENONE WITH 1, 2-ETHYLENEDIAMINE

Schiff bases synthesized by the condensation between diamines with aromatic or aliphatic carbonyl compounds correspond to a significant group of chelating ligands, which were used to synthesize a number of metal complexes, which have been studied extensively[1-8]. A search through the literature[9-18] revealed that no study has been done on transition metal complexes of the Schiff base derived from *o*-vanillin, *o*-hydroxyacetophenone and a diamine. The present study involves the preparation, identification and characterization of a new tetradentate dianionic Schiff base derived from the condensation of *o*-vanillin and *o*-hydroxyacetophenone with 1, 2-ethylenediamine in 1:1:1 molar ratio and its seven metal complexes. The choice of these carbonyl compounds in the present investigation has been made due to their diverse biological activities.

A. EXPERIMENTAL

1. Materials and methods

Specifications regarding the reagents used, the procedural details adopted for synthesis and characterization of the ligand and the complexes are given in the Chapter II. For the preparation of the ligand, *o*-vanillin, *o*-hydroxyacetophenone and 1,2-ethylenedaimine were used. The metal salts used in this study were of BDH AnalaR quality. Mainly chlorides and sulphates of Cr(III), Mn(II), Fe(III), Co(III), Ni(II), Cu(II) and Zn(II) were used for the synthesis of the complexes.

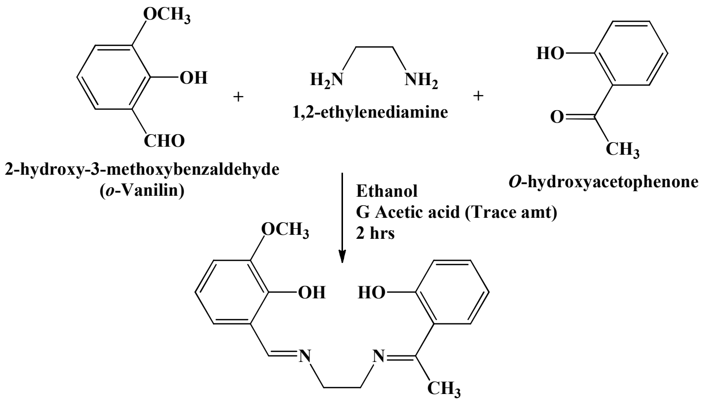
The solvents used for the synthesis, extraction and recrystalization of the ligands and the complexes were ethanol, methanol, chloroform, DMF, DMSO, petroleum benzene, diethyl ether, etc. Commercially available solvents, like ethanol and methanol were purified by standard methods[33]. Others were E. Merck grade reagents and were used as such. The solvents, such as methanol and DMF used for spectral- and conductivity measurements were of spectroscopic grade.

2. Synthesis

a. *o*-Vanillin -(1,2-ethylenediimine)o-hydroxyacetophenone (VEH)

O-vanillin (0.025 mol) and *o*-hydroxyacetophenone (0.025 mol) in minimum amount of ethanol were added to a solution of 1, 2-ethylenediamine (0.025 mol) in ethanol in a 250 ml round bottom flask. The mixture was refluxed for 2 h. The completion of the reactions was monitored by thin-layer chromatography (TLC) on pre-coated silica gel F_{254} plates from Merck. After the completion of the reaction, the mixture was slowly cooled in an ice bath. The orange-yellow crystals formed were filtered, washed with ethanol, recrystallized from DMSO and dried over anhydrous calcium chloride. (**Scheme. 1**)

Scheme. 1: Synthesis of the ligand, o-vanillin-(1,2-ethylenediimine)o-hydroxyacetophenone (VEH)



***The systematic name of the compound is: 2-((E)-((2-((E)-(1-(2-hydroxyphenyl)ethylidene)amino)ethyl)imino)methyl)-6-methoxyphenol. But for the sake of convenience the name '*O*-vanillin-(1, 2-ethylenediimine)*o*-hydroxyacetophenone" and the short form 'VEH' are adopted in this thesis.**

b. Complexes

Methanolic solution of the metal salt (0.005 mol in 20 ml ethanol) was added to a solution of the ligand (0.005 mol in 20 ml DMSO) and the mixture was refluxed for about 4 h. It was then cooled and allowed to evaporate the solvent to reduce approximately half of the total volume. The solid complexes formed was filtered off, washed several times with petroleum benzene and finally with methanol and was dried over anhydrous calcium chloride. (**Table. 1**)

Table. 1: Physical properties of the synthesized complexes

Si. No	Metal Salt Used	Color	Melting point
1.	$CrCl_3.2H_2O$	Green	<300°C
2.	$MnSO_4.5H_2O$	Brownish red	<300°C
3.	$FeCl_3.6H_2O$	Pale Red	<300°C
4.	$CoCl_2.5H_2O$	Light red	298°C
5.	$NiCl_2.2H_2O$	Greenish brown	290^0C
6.	$CuCl_2.2H_2O$	Blue	<300°C
7.	$ZnSO_4.7H_2O$	White	295^0C

B. RESULTS AND DISCUSSION

The data obtained from the analytical-and physico-chemical studies have been correlated to explain the properties, structures and bondings of the compounds.

1. Characterization of the ligand

The Schiff base ligand derived from *o*-vanillin, *o*-hydroxyacetaphenone and 1,2-ethylenediamine was orange yellow coloured crystals, soluble in non-polar solvents like DMSO, benzene, etc. The homogeneity and purity of the ligand were tested by TLC technique. Melting point (180^0C) of the ligand was determined using a Fisher-Johns apparatus. The ligand was characterized by elemental analysis, IR- ^1H NMR- and UV-Vis spectral studies.

a. Elemental analysis

The Schiff base ligand, VEH was subjected to elemental analysis on a CHN-O instrument. The experimentally found out- and calculated percentages of C, H and N were in good agreement, confirming its molecular formula, $C_{18}H_{25}N_2O_3$. (**Table. 2**)

Table. 2: Elemental analysis of the ligand, VEH

Ligand	Carbon (%)		Hydrogen (%)		Nitrogen (%)	
	Found	Calculated	Found	Calculated	Found	Calculated
$C_{18}H_{20}N_2O_3$	70.11	69.21	5.98	6.45	9.01	8.97

b. ^{1}H NMR spectrum

The ^{1}H NMR spectrum of the ligand, VEH was recorded in DMSO-d_6. Singlets observed at 4.56–4.65 ppm were assigned to -OH protons of *o*-vanillinn and *o*-hydroxyacetophenone moieties. The signals appeared at 6.90-7.49 and 6.78-7.22 ppm may be attributed to the protons of the two aromatic groups. There was a singlet at 3.25 ppm which may be attributed to –OCH_3 protons. The triplet peaks appeared at 2.67 ppm and a singlet present at 1.80 ppm may be attributed, respectively, to the –CH_2- and –CH_3 protons of ethylenediimine and o-hydroxyacetophenone moiety near –C=N group. A sharp peak appeared at 7.85 was due to –CH=N- proton near o-vanillin moiety. (**Table. 3**)

Fig. 1: ^{1}H NMR spectrum of ligand, VEH

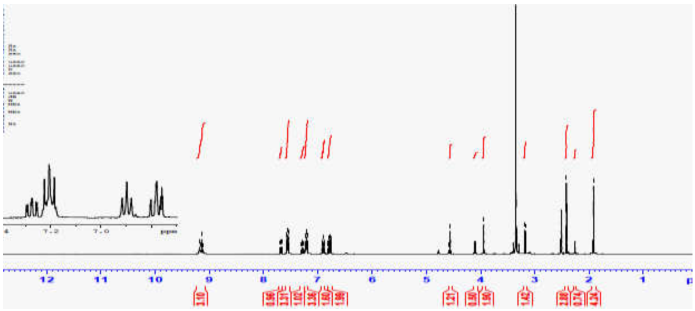


Table. 3: ^{1}H NMR data of ligand, VEH

Si.No.	Chemical shift (ppm)	Assignment
1.	8.45(s)*	-CH=N- proton
2.	6.78-7.22 (m) 6.90-7.49 (m)	Aromatic protons
3.	3.25 (s)	$-OCH_3$ active methylene proton
4.	4.56 (s), 4.65(s)	2-OH proton
5.	1.80 (q)	$-CH_3$ proton
6.	2.67 (t)	2 $-CH_2$ protons between imine group

*s= singlet, t= triplet, q= quartet

c. IR spectrum

The IR spectrum of the ligand, VEH showed a number of absorption bands, which were characteristics of various functional groups present in it. Assignments were given on the basis of analogous structures, known earlier[19,20]. The probable assignments are given in **Table. 4 & Fig. 2**.

The bands present at 1630 and 1234 cm^{-1} were assigned to the $\nu_{-C=N}$ and $\nu_{=N-C-}$, respectively. The band at 3050 cm^{-1} may be assigned to the aromatic ν_{-CH} and that at 2915 cm^{-1} to the ν_{-CH} of the methylene group. The band at 2959 and 2940 cm^{-1} were due to the symmetric- and asymmetric stretching vibrations of $>CH_2$ group. A sharp band at 3550 cm^{-1} may be due to ν_{-OH}. The characteristic bands due to the stretching of >C=O of the *o*-vanillin and *o*-hydroxyacetophenone, at the range 1660-1668 cm^{-1} were not present in the spectrum, which indicated that the condensation was complete. A sharp band at 1215 cm^{-1} was due to the ν_{C-O} of ethoxy group.

Fig. 2: IR spectrum of the ligand, VEH

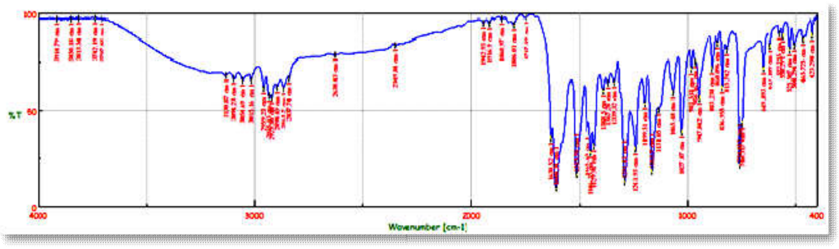


Table. 4: Significant IR bands of ligand, VEH and their assignments

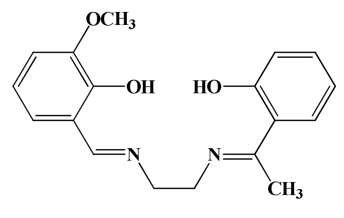
Band frequency* (cm^{-1})	Assignment
3550	ν_{-OH} phenolic
1630	$\nu_{>C=N}$ of o-hydroxyacetophenone moiety
3050 2915	ν aromatic –CH ν_{-CH2} (Methylene)
1234	$\nu_{>C-N-}$
1616 1559	δ in plane –CH (aromatic)
1215	ν_{-CO-} (ethoxy)
874 819	δ out of plane –CH (aromatic)

d. Electronic spectrum

The electronic spectrum of the ligand was recorded in DMSO. The band at 35714 cm^{-1} attributed to $\pi \rightarrow \pi^*$ transition of the aromatic part of the ligand specifically. The band at 24875 cm^{-1}nm may be due to the $n \rightarrow \pi^*$ transition of the non-bonding electrons present on the oxygen of the keto (>C=O) groups and nitrogen of the azomethine (C=N) groups in the ligands[21].

On the basis of above experimental data, the probable structure of the ligand, VEH is given below, **Fig. 3**

Fig. 3: Structure of the ligand, VEH



2. Characterization of complexes

a. Analytical data

All the complexes, except that of Zn(II) were found to be coloured, non-hygroscopic and photo-stable. They were soluble in DMF and DMSO but only sparingly soluble in common organic solvents. The data obtained from analytical-and molar conductance studies in DMF showed that the complexes have the formulae as shown in **Table. 5**. The magnetic -and various spectral data also confirmed the suggested molecular formulae.

Table. 5, Analytical data of complexes

Empirical Formula	F^*. Wt	Elemental %, Found (Calculated)				
		M	C	H	N	Anion
$CrC_{18}H_{20}N_2O_4Cl$	384	12.90 (13.51)	45.55 (46.82)	6.04 (6.55)	8.01 (7.28)	10.01 (9.21)
$MnC_{18}H_{22}N_2O_5$	370	15.61 (14.84)	49.20 (48.68)	6.95 (7.35)	8.01 (7.56)	----
$FeC_{18}H_{20}N_2O_4Cl$	388	13.79 (14.37)	47.16 (46.55)	5.80 (6.48)	6.77 (7.21)	10.11 (9.12)
$CoC_{18}H_{22}N_2O_5$	374	16.02 (15.74)	49.00 (48.13)	8.75 (7.27)	8.06 (7.48)	---
$NiC_{18}H_{22}N_2O_5$	373	16.22 (15.69)	47.25 (48.16)	6.69 (7.28)	6.88 (7.49)	---
$CuC_{18}H_{22}N_2O_5$	378	16.78 (16.77)	46.47 (47.54)	6.31 (7.18)	8.05 (7.39)	---
$ZnC_{18}H_{22}N_2O_5$	343	18.28 (17.17)	48.03 (47.32)	6.97 (7.15)	8.05 (7.36)	---

L2H = $C_{18}H_{25}N_3O_3$

b. Molar Conductance

Molar conductance data are exploited to determine electrolytic and non-electrolytic character of the metal complexes. Besides, molar conductance data have been used to predict the structures of metal complexes. The molar conductances at room temperature were determined using 10^{-3} M solutions of the complexes in DMSO and are given in the **Table. 6**. The molar conductance values were in the range 10-25 $\Omega^{-1}mol^{-1}cm^2$, indicating the non-electrolytic nature of the complexes, accordingly, they were assigned formulae. Analytical data and spectral studies also supported the suggested formulae. (**Table. 6**)

Table. 6: Molar conductance complexes in DMSO		
Si No:	Complexes	Λ_m ($\Omega^{-1}mol^{-1}cm^2$)
1.	$[CrL(H_2O)Cl]$	10
2.	$[MnL(H_2O)_2]$	25
3.	$[FeL(H_2O)_2Cl]$	15
4.	$[CoL(H_2O)_2]$	20
5.	$[NiL(H_2O)_2]$	18
6.	$[CuL(H_2O)_2]$	16
7.	$[ZnL(H_2O)_2]$	11
L = $C_{18}H_{23}N_3O_3$		

c. Magnetic moment

The magnetic susceptibilities of the complexes were measured at room temperature using a Gouy balance. $Hg[Co(NCS)_4]$ was used as the calibarant. Diamagnetic corrections were applied using Pascal constants for atoms and structural units of the complexes. The magnetic susceptibilities, diamagnetic corrections and the effective magnetic moment values were calculated. The corrected magnetic susceptibilities are given in the **Table. 7**

In the present investigation, the VEH complex of Cr(III) showed a magnetic moment value of 3.82 B.M., which indicated its octahedral geometry. The magnetic moments of a number of Schiff base complexes of Mn(II) have been found to be significantly below spin-only value. These complexes may not be magnetically dilute and these is no obvious explanation for these low magnetic moment data. In the present case, $[MnL(H_2O)_2]$ complex showed a value at 5.70 B.M indicating its octahedral geometry[22-24].

Fe(III) complex of VEH registered a magnetic moment value at 5.90 B.M. indicating its octahedral geometry. In the present investigation, the $[CoL(H_2O)_2]$ registered a magnetic moment value of 5.11 B.M., which indicated its octahedral geometry. The VEH Schiff base complex of Ni(II) investigated here registered a magnetic moment value 3.30 B.M., indicating its octahedral geometry. Cu(II) complex registered a magnetic moment value of 1.91 B.M., indicating its octahedral geometry. (**Table. 7**)

Table. 7: Magnetic moment data of complexes

Si No:	Complexes	μ_{eff} (B.M)
1.	$[CrL(H_2O)Cl]$	3.82
2.	$[MnL(H_2O)_2]$	5.70
3.	$[Fe(LH_2)Cl_3]$	5.90
4.	$[CoL(H_2O)_2]$	5.11
5.	$[NiL(H_2O)_2]$	3.30
6.	$[CuL(H_2O)_2]$	1.91

μ_{eff} = Effective magnetic moment, B.M = Bohr magneton

d. Electronic Spectra

The study of electron absorption spectra, especially crystal field spectra of coordination complexes, provides important information such as the magnitude of energy gaps between the ground- and the excited electronic energy states of the metal ions in the complexes, colors of the complexes, the extend of covalent character in metal-ligand bonds, the geometry of the complexes, the position of metals and the ligands in the spectrochemical- and nephelauxetic series, etc[25].

In the present case, in the electronic spectrum of Cr(III) complex, two band observed at 17,400 and 22,500 cm^{-1} and were assigned to the $^4A_{2g} \rightarrow {}^4T_1$ (P) and the $^4A_{2g} \rightarrow {}^4T_{2g}$ transition characteristic of octahedral geometry[26-28].

The spectra of the Mn(II) complexes show a number weak bands around the region, 18,000 - 25,000 cm^{-1} which were assigned to d-d transitions in an octahedral field. $[MnL(H_2O)_2]$ exhibited three electronic spectral bands at 14,600 cm^{-1}, 19,900 cm^{-1} and 23,990 cm^{-1} which were assigned to the $^6A_{1g} \rightarrow {}^4T_{1g}$, $^6A_{1g} \rightarrow {}^4T_{2g}$ and $^6A_{1g} \rightarrow {}^4E_g$ transitions. The brown color of the complex may also supported its octahedral nature[28].

In the present investigation, $[FeL(H_2O)Cl]$ complex showed two bands, one at 25,100 cm^{-1} and a broad one at 19,600 cm^{-1}. These were assigned to d-d transitions of Fe(III) ion in an octahedral field[29-33].

In the present investigation, the spectrum of Co(II) complex showed three intense transitions. Bands were present at 8,850, 14,900 and 24,500 cm^{-1} and were assigned, respectively to the $^4T_{1g}\rightarrow{}^4T_{2g}$ (ν_1), $^4T_{1g}\rightarrow{}^4A_{2g}$ (ν_1) and $^4T_{1g}\rightarrow{}^4T_{1g}$ (P) (ν_1)[34] transitions of an octahedral Co(II) complex.

The VEH Schiff base complex of Ni(II), investigated here showed three transitions corresponding to octahedral geometry. Bands were identified at 8,710, 13,840 and 24,300 cm^{-1} and were assigned, respectively, to the $^3A_{2g}\rightarrow{}^3T_{2g}$ (F), $^3A_{2g}\rightarrow{}^3T_{1g}$(F) and $^3A_{2g}\rightarrow{}^3T_{1g}$ (P). The ratio of wave numbers of the transitions assigned as $^3A_{2g}\rightarrow{}^3T_{2g}$ (F) and $^3A_{2g}\rightarrow{}^3T_{1g}$(F) was found to be 1.6 confirming its octahedral geometry.

The six coordinated Cu(II) belongs to d^9 system. We expect a single absorption band representing the transition, $^2E_g\rightarrow{}^2T_{2g}$. The pale blue $[Cu(H_2O)_6]Cl_2$ complex shows a broad band with two maxima ~ 11,000 cm^{-1} Cu(II) is very sensitive to the Jhan-Teller distortion. In the present investigation, the spectrum of Cu(II) VEH complex exhibited broad at 13,300 cm^{-1} and was assigned to the $^2E_g\rightarrow{}^2T_{2g}$[34] transition indicating its octahedral geometry. (**Table. 8**)

Table. 8: Electronic spectra of complexes.

Si. No:	Complexes	Bands (cm^{-1})	Assignments	Geometry
2.	$[CrL(H_2O)Cl]$	17,400	$^4A_{2g}\rightarrow{}^4T_1$ (P)	Octahedral
		22,500	$^4A_{2g}\rightarrow{}^4T_{2g}$	
3.	$[MnL(H_2O)_2]$	14,600	$^6A_{1g}\rightarrow{}^4T_{1g}$	Octahedral
		19,900	$^6A_{1g}\rightarrow{}^4T_{2g}$	
		23,990	$^6A_{1g}\rightarrow{}^4E_g$	
4.	$[Fe(LH)Cl_3]$	19,600	$^6A_{1g}\rightarrow{}^4T_{2g}$	Octahedral
		25,100	CT	
5.	$[CoL(H_2O)_2]$	8,850	$^4T_{1g}\rightarrow{}^4T_{2g}$	octahedral
		14,790	$^4T_{1g}\rightarrow{}^4A_{2g}$	
		24,500	$^4T_{1g}\rightarrow{}^4T_{1g}$ (P)	
6.	$[NiL(H_2O)_2]$	8,710	$^3A_{2g}\rightarrow{}^3T_{2g}$	Octahedral
		13,840	$^3A_{2g}\rightarrow{}^3T_{1g}$	
		24,300	$^3A_{2g}\rightarrow{}^3T_{1g}$	
7.	$[CuL(H_2O)_2]$	13,300	$^2E_g\rightarrow{}^2T_{2g}$	octahedral

e. IR spectra

IR spectral technique is useful for the identification and characterization of metal complexes and in assigning structures and geometries to them. The important bands and their probable assignments are given in **Table. 9**.

A bands of medium intensities at 1630 cm^{-1} in the spectrum of ligand may be assigned to $\mathbf{v}_{C=N}$. However, the spectra of the complexes, this bands were found to be shifted to lower frequency region by a few cm^{-1}, indicated the participation of azomethine nitrogen in coordination. A band at 3550 cm^{-1} in the spectrum of ligand may be assigned to phenolic $\mathbf{v}\text{-}_{\mathbf{OH}}$ of *o*-hydroxyacetopheneone and *o*-vanillin. Disappearance of this band in the spectra of all the complexes indicated that the chelation took place through the deprotonated –OH.

The band at 3050 cm^{-1} may be assigned to the aromatic –CH stretching and that at 2915 cm^{-1} to the –CH stretching of the methylene group. Sharp bands at 1215 and 1050 cm^{-1} were characteristic peaks of $\mathbf{v}_{C\text{-}O}$ of ethoxy group. Broad bands at ~ 3500-3460 cm^{-1} in the spectra of Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) complexes was attributed to the hydroxyl stretching modes of water molecules. In addition , strong bands at ~ 860-980 and ~ 640 cm^{-1} suggested that the water molecules were coordinated.[65] Medium bands in the ranges 515-550 and 405-440 cm^{-1} in the spectra of all the complexes may be assigned[35] to $\mathbf{v}_{(\mathbf{M\text{-}N\text{-}})}$ and $\mathbf{v}_{(\mathbf{M\text{-}O\text{-}})}$, respectively. Band in the range 410-430 cm^{-1} in the spectra of Cr(III) and Fe(III) complex indicated the presence of M-Cl bonds. (**Table. 9 & Fig. 4-8**)

Table. 9: Significant IR bands of complexes and their assignments						
Compounds	Assignments and band frequencies (cm^{-1})					
	$\nu_{-C=N}$	ν_{-OH} (H_2O)	ν_{M-N}	ν_{M-O}	ν_{M-Cl}	H_2O coordination $\rho_{\text{rock and wagg}}$
VEH (LH_2)	1630 1621	3550	-----	---	----	----
[CrL(H_2O)Cl]	1620 1611	3405	521	465	416	870m, 663m
[MnL(H_2O)$_2$]	1619 1609	3400	520	461	---	955m, 620m
[FeL(H_2O)Cl]	1618 1610	3510	525	475	415	986m, 665m
[CoL(H_2O)$_2$]	1615 1605	3350	518	478	----	970m, 656m
[NiL(H_2O)$_2$]	1621 1612	3400	520	478	---	980m, 653m
[CuL(H_2O)$_2$]	1616 1606	3400	519	470	----	973m, 652m
[ZnL(H_2O)$_2$]	1622 1605	3445	523	471	----	984m, 650m

Fig. 4: IR spectrum of Mn(II) complex

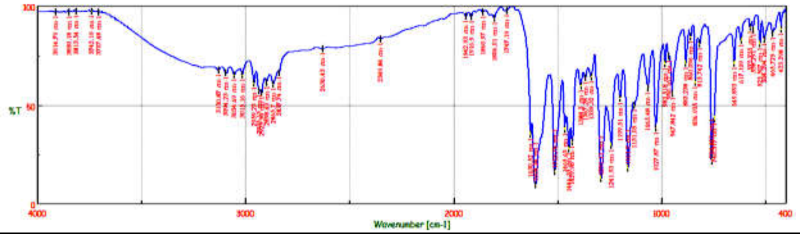


Fig. 5: IR spectrum of Co(II) complex

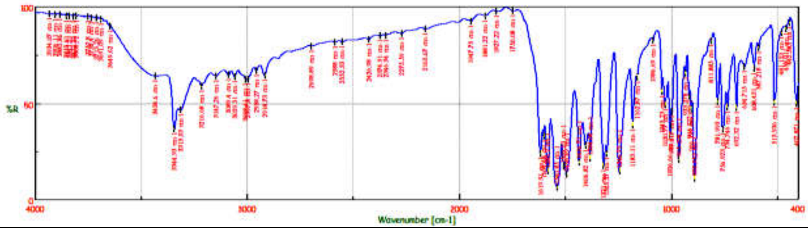


Fig. 6: IR spectrum of Ni(II) complex

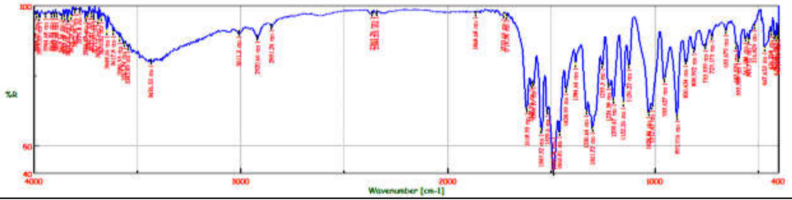


Fig. 7: IR spectrum of Cu(II) complex

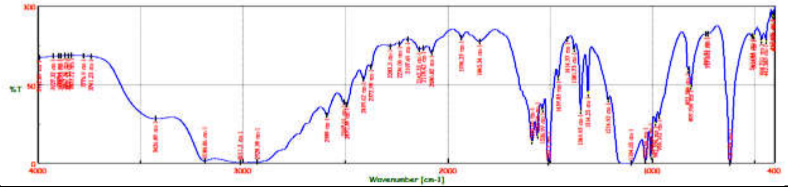
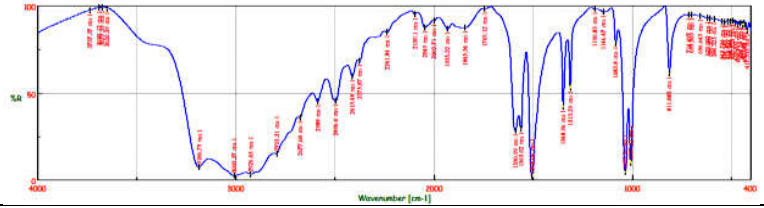


Fig. 8: IR spectrum of Zn(II) complex



On the basis of the above experimental data, the probable structures of the Schiff base ligand, VEH and its complexes of Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) are given below: (**Fig. 9-12**)

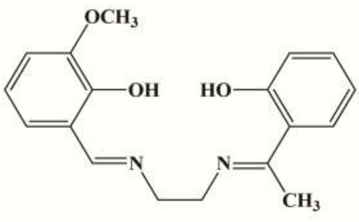
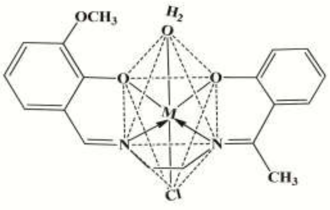
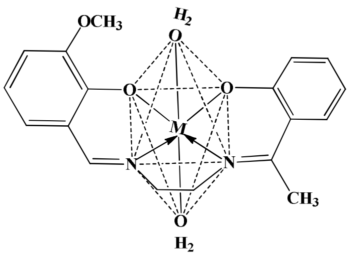
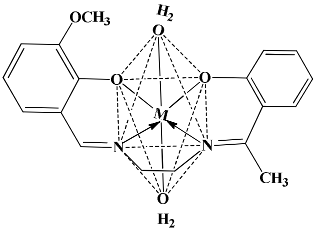
Fig. 9: Structure of the ligand, VEH	**Fig. 10: Structure of [ML(H_2O)Cl], where M = Cr(III), Fe(III)**
	

Fig. 11: Structure of [ML(H_2O)$_2$], where M = Mn(II) and Co(II),	**Fig. 12: Structure of [ML(H_2O)$_2$], where M = Ni(II), Cu(II) and Zn(II)**
	

C. CONCLUSIONS

Coordination complexes of Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) with a tetradentate ONNO Schiff base ligand, *o*-vanillin-(1,2-ethylenediimine)*o*-hydroxyacetophenone (L2H) have been prepared and their physico-chemical properties have been studied. The ligand, o-vanillin-(1,2-ethylenediimine)-o-hydroxyacetophenone (VEH) was synthesized by the condensation reaction of *o*-vanillin and *o*-hydroxyacetophenone with 1,2-ethylenediamine in 1:1:1 molar ratio. The complexes have the general formulae, [CrL(H_2O)Cl], [MnL(H_2O)$_2$], [FeL(H_2O)Cl], [CoL(H_2O)$_2$], [NiL(H_2O)$_2$], [CuL(H_2O)$_2$] and [ZnL(H_2O)$_2$]. Based on the analytical, magnetic and various spectral studies, geometries have been assigned to these complexes. All the aqua complexes were found to be octahedral.

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PART-II

BIOTOXIC EVALUATION

Chapter IX

ANTIMICROBIAL STUDIES OF THE LIGANDS AND THEIR COMPLEXES

A. INTRODUCTION

Microorganisms are evolved to use other organisms including humans as habitats. Microbes can be found in various parts of human body, such as, skin, intestines and mouth. These microbes begin to colonize human shortly after birth. As the microbes establish themselves, they contribute to the developments of the body`s immune system. Those microbes that inhabit the large intestine help the body digest food and produce Vitamin B and- K. In these and other ways, microbes help to maintain the health and well being of their human hosts.

The diversity of cellular microorganism is best exemplified by their metabolic capabilities, and human beings have learned to harness the metabolism of microbes to achieve a verity of goals. Microbes are used to produce bread, cheese, beer, antibiotics, vaccines and many other valuable products. Although most microbes play beneficial or benign roles, some harm the large organisms they live with, causing disease in both animals and plants.

1. Schiff base metal complexes as antimicrobial agents

Schiff bases and their metal complexes have vide verity applications, such as, in the treatment of cancer[1] and as bactericides[2], antiviral agents[3] and fungicides[4,5].

Mehmet TuÈmer *et.al*[6] prepared metal complexes of three novel tridentate Schiff base ligands derived from 3-hydroxysalicylaldehyde, 4-hydroxysalicylaldehyde and 5-bromosalicylaldehyde with N-(pyridyl)-2-hydroxy

3-methoxy-5-aminobenzylamine. Antimicrobial activities of these ligands and their complexes have been tested against some selected bacteria.

Rehman *et.al*[7] reported the synthesis of a novel Schiff base derived from aniline and salicylaldehyde and its Co(II), Mn(II) and Zn(II) complexes. Screening of these compounds showed that the complexes exhibited potential activity against all microorganisms.

Fe(III), Ni(II) and Mn(III) complexes of a hepta-dentate Schiff-base ligand have been prepared by R. R. Khojasteh *et.al*[8]. The ligand was derived from acetylacetone and *tris*-(2-aminoethyl)amine. *In vitro* biological screening studies of these compounds were carried out on Gram-negative bacteria, *Escherichia coli, Pseudomonas aeruginosa* and Gram-positive bacteria, *Staphylococcus aureus, Bacillus cereus* by the disc diffusion- and micro-broth dilution methods. All these compounds have shown potent antibacterial activity compared to the standards. The metal complexes have shown to possess more antibacterial activity than the free Schiff base.

Gupta Fahmi[9] reported two novel Schiff base ligands, 1-acetylferrocenehydrazine carboxamide and 1-acetylferrocenehydrazine carbothioamide and their Ni(II) and Co(II) complexes. The metal complexes have shown enhanced the antibacterial- and antifungal activity against microbial strains in comparison with the free ligands. Thus, they may find application as new antimicrobial agents after further studies.

The Potassium salts of the novel Schiff bases, salicylidene-DL-alanine, *bis*-(benzylidene)ethylenediamine and thiophene-*o*-carboxaldene-*p*-toluidine and their Mn(II), Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) complexes were synthesized by Parekh *et.al*[10]. All these complexes, fungicides and ligands were screened for their antifungal activities against *Aspergillus niger*, *Fusarium oxysporum* and *Aspergillus flavus* using a plate poison technique. The complexes showed higher activities than the free ligands and control (DMSO). They showed moderately higher activities against the standard drugs, bavistin and emcarb.

A series of complexes of Zn(II) have been prepared by Bagihalli *et.al*[11]with novel bio-active Schiff bases derived from the condensation of 3-substituted-4-amino-5-mercapto-1,2,4-triazole with 8-formyl-7-hydroxy-4-methylcoumarin. All these Schiff bases and their complexes have been screened for their antibacterial- (*Escherichia. coli, S. aureus, S. pyogenes, P. aeruginosa and Salmonella typhi*) and antifungal (*Aspergillus niger, Aspergillus flavus and cladosporium*) activities by MIC (minimum inhibitory concentration) method. The brine shrimp bioassays were also carried out to study their *in vitro* cytotoxic properties. It was observed that the ligands showed moderate antifungal activities against *A. flavus* and *A. Niger* and high activity towards *Cladosporium.* The complexes showed high activities against *A. niger*, *Cladosporium* and *A. flavus.* However, some of these complexes were inactive against *A. Flavus* and *A. niger* at low concentration.

Nahid Nishat *et.al*[12] reported complexes of Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) with a new polymeric Schiff base containing formaldehyde and piperazine moieties. All the complexes exhibited good activities against three types of bacteria and two types of fungi. The antimicrobial activities were determined by using agar well diffusion method with 100 µg/ml concentrations of the polymeric metal complexes. The results of screening studies indicated that the Cu(II) complexes exhibited a higher activities than the other metal complexes. The result may be due to the higher stability of the Cu(II) complexes.

Nahid Nishat[13] prepared a novel Schiff base by the condensation reaction of ethanedihydrazide with 2-hydroxybenzaldehyde. This monomeric Schiff base was polymerized with formaldehyde and barbituric acid to form a polymeric Schiff base ligand. The ligand and its polymeric metal complexes were screened against bacterial species, *Escherichia coli, Staphylococcus aureus* and *Bacillus* *subtilis* and fungal species, *Aspergillus flavus, Candida albicans* and *A. niger*. The activity data revealed that the metal complexes were more potent than the parent Schiff base. Polymeric complex of Cu(II) showed better antibacterial activity and more thermal stability than the other complexes. Because of the more toxic behaviour of the Cu(II) complex, they suggested that it may be used in antifungal- and antifouling coatings.

The reactions of Ru(II) complexes, [RuHCl(CO)(PPh3)2(B)] [B = PPh3, pyridine (py) or piperidine (pip)], with bidentate Schiff base ligands derived by condensing salicylaldehyde with aniline, *o*-, *m*- or p-toluidine have been carried out by Dharmaraj *et.al*[14]. The Schiff bases and the new complexes were tested *in vitro* to evaluate their activities against the fungus, *Aspergillus avus*. The results showed that the ruthenium chelates were more toxic as compared with their parent ligands against the same microbe and under the identical experimental conditions. The higher antifungal activities of the metal chelates may be due to the interference of the metal ions in the normal cell process.

Parekh *et.al*[15] reported the mixed-ligand complexes of Mn(II), Co(II), Ni(II), Cu(II), Zn(II), and Cd(II) with bio-active novel Schiff bases ligands, potassium salt of *o*–hydroxyacetophenoneglycine and bis(benzylidene) ethylenediamine or thiophene-*o*-carboxaldene-*p*-toluidine. The mixed-ligand complexes showed better antifungal activities as compared to the free ligands, metal salts and the control (dimethylsulfoxide) but showed only moderate activities as compared to the standard fungicides (bavistin and emcarb).

The coordination complexes of VO(II), Co(II), Ni(II) and Cu(II) with the Schiff bases from 3-bromobenzaldehyde/3-chlorobenzaldehyde with 2-aminophenol have been synthesized by A.P. Mishra *et.al*[16]. The *in vitro* biological screening test of these compounds were done against the bacteria, *Escherichia coli, Staphylococcus aureus* and *Streptococcus fecalis* and the fungi, *Aspergillus niger, Trichoderma polysporum* and *Candida albicans* by serial dilution method.

A comparative study of the MIC values of the Schiff bases and their Co(II) and Cu(II) complexes indicated that the metal complexes exhibited higher antimicrobial activities than the free ligand. In some cases the Schiff bases were more active than their metal complexes against bacteria.

B. SCOPE OF THE PRESENT INVESTIGATION

Schiff bases have shown to exhibit a broad spectrum of bioactivities including antibacterial, antifungal anti-proliferative, anti-inflammatory, antiviral, and antipyretic properties. The presence imine (>C=N-) group in such compounds has been shown to be critical to their biological activities[17].

In our present investigation the antibacterial- and antifungal activities some of the novel Schiff base ligands, AcEE and VEAc and their transition metal complexes were studied and the results were analysed. The methods adopted and the observations are presented in the subsequent sub-sections.

Sub-section I

ANTIBACTERIAL ACTIVITIES OF THE LIGANDS, AcEE AND VEAc AND THEIR METAL COMPLEXES

Screening of antibacterial activities of the ligand, AcEE and its Fe(III), Co(II), Ni(II) and Cu(II) complexes and the ligand, VEAc and its complexes of Co(II), Ni(II), Cu(II) and Zn(II) were carried out using Kirby Bauer or Disc Diffusion method.

A. MATERIALS AND METHODS

1. Bacterial cultures used

The bacterial cultures used in the present investigation were three gram positive bacteria; *Bacillus, Staphylococcus, Streptococcus* and three gram negative bacteria; *Escherichia coli, Klebsiella and Pseudomonas*. The pure cultures were purchased from Microbial Type Culture Collection and Gene Bank, Institute of Microbial Technology, Chandigarh, India.

2. Media used

Nutrient Broth

(HiMedia Laboratories Pvt Ltd, Mumbai)

Peptic digest of animal tissue : 5 gram
Sodium Chloride : 5 gram
Yeast extrsact : 1.5 gram
Distilled water : 1000 ml (p^H – 7.4)

Nutrient Agar

(HiMedia Laboratories Pvt Ltd, Mumbai)

Peptic digest of animal tissue : 5 gram
Sodium Chloride : 5 gram

Yeast extrsact : 1.5 gram

Distilled water : 1000 ml (p^H – 7.4)

Agar : 15 gram

3. Antibacterial activity by Disc Diffusion or Kirby Bauer Method

The disc diffusion agar method tests the effectiveness of the antibiotics on a specific microorganism. An agar plate is first spread with bacteria and then paper discs containing antibiotics are added to it. The bacteria are allowed to grow on the agar media. The widening of space around every antibiotic plate indicates the lethality of that antibiotic on the bacteria in question.

In the present study, antibacterial tests were carried out by disc diffusion method[18] (with some modifications). The cultures (mentioned above) were maintained in nutrient broth. Each culture was uniformly spread on Nutrient agar plate using sterile swab. Sterile filter paper discs of 3 mm diameter were placed on the surface of Nutrient agar plates at a distance of 2 cm from each other using sterile forceps. DMSO (2%) was used to dissolve the drug, which was found to have no adverse effect on the bacterial cultures. Drugs of different concentrations (1 and 5 mg/ml) were added on each disc with a micropipette. Disc with DMSO but without drug was used as a control. The plates were then incubated at 37^0C for 24 hours. After incubation, the zone diameter was measured. The larger diameters shown by the compounds than the control indicate their antifungal activities.

B. RESULTS

1. Antibacterial activities of AcEE and its Fe(III), Co(II), Ni(II) and Cu(II) complexes

After incubation, the zone diameter (in millimetre) of AcEE (**Fig. 1)** and its metal complexes (**Fig. 2**)were measured. The results of disc diffusion method are shown in **Tables 1 & 2**. The results revealed that the complexes of AcEE showed antibacterial activities against the tested strains in a dose dependent manner. However, the free ligand, AcEE was not found to possess any antibacterial activity.

Fig. 1. Ligand, AcEE

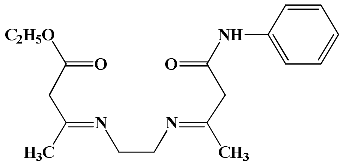


Fig. 2: Structure of Schiff base metal complexes of AcEE: A: Fe(III), B: Co(II), C: Ni(II) and D: Cu(II)

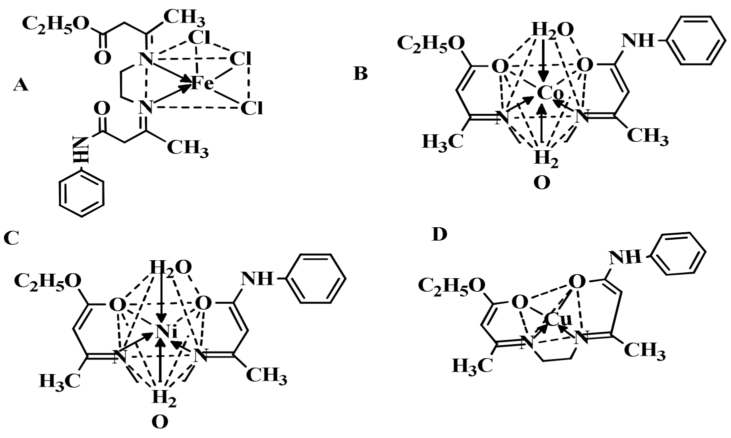


Table. 1 Antibacterial activity of AcEE and its complexes in 1mg/ml					
Microorganisms	**Zone diameter (mm)**				
	AcEE	**Fe(III)**	**Co(II)**	**Ni(II)**	**Cu(II)**
Stephylococcus	**Nil**	**14**	**11**	**8**	**16**
Streptococcus	**Nil**	**9**	**8**	**--**	**15**
Bacillus	**Nil**	**10**	**10**	**9**	**13**
E. Coli	**Nil**	**10**	**8**	**10**	**10**
Klebsiella	**Nil**	**8**	**8**	**7**	**9**
Psuedomonas	**Nil**	**--**	**--**	**7**	**8**
DMSO = no activity					

Table. 2. Antibacterial activity of AcEE and its complexes in 5mg/ml					
Microorganisms	**Zone diameter (mm)**				
	AcEE	**Fe(III)**	**Co(II)**	**Ni(II)**	**Cu(II)**
Stephylococcus	**Nil**	**18**	**16**	**18**	**20**
Streptococcus	**Nil**	**17**	**15**	**--**	**22**
Bacillus	**Nil**	**12**	**10**	**15**	**22**
E. Coli	**Nil**	**15**	**17**	**10**	**18**
Klebsiella	**Nil**	**15**	**14**	**14**	**15**
Psuedomonas	**Nil**	**8**	**--**	**10**	**10**
DMSO = no activity					

2. Antibacterial activities of VEAc and its Co(II), Ni(II), Cu(II) and Zn(II) complexes

After the incubation, the zone diameter in (millimetre) of VEAc (**Fig. 3)** and its complexes with Co(II), Ni(II), Cu(II) and Zn(II) were measured. The results of disc diffusion method are shown in **Tables. 3 & 4**. The experimental results indicated that the complexes of VEAc showed dose dependent activities against the tested strains of bacteria. However, the free ligand, VEAc was not found to possess any antibacterial activity.

Fig. 3. Ligand, VEAc

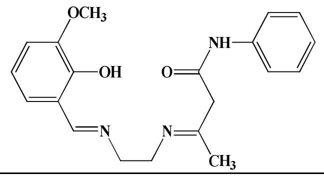


Fig. 4: Structure of Schiff base metal complexes of VEAc: A: Co(II), B: Ni(II), C: Cu(II) and D: Zn(II)

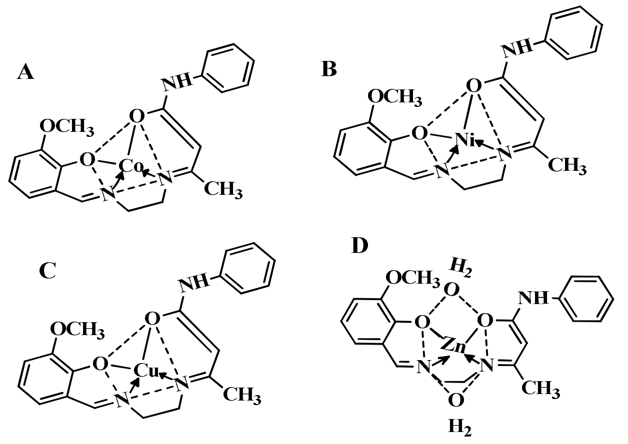


Table. 3, Antibacterial activity of VEAc and its complexes in 1mg/ml					
Microorganisms	**Zone diameter (mm)**				
	VEAc	**Co(II)**	**Ni(II)**	**Cu(II)**	**Zn(II)**
Stephylococcus	**Nil**	**--**	**7**	**20**	**10**
Streptococcus	**Nil**	**10**	**6**	**15**	**--**
Bacillus	**Nil**	**--**	**--**	**25**	**10**
E. Coli	**Nil**	**--**	**6**	**40**	**15**
Klebsiella	**Nil**	**8**	**--**	**15**	**15**
Psuedomonas	**Nil**	**--**	**--**	**20**	**10**
DMSO = no activity					

Table. 4, Antibacterial activity of VEAc and its complexes in 5 mg/ml					
Microorganisms	**Zone diameter (mm)**				
	VEAc	**Co(II)**	**Ni(II)**	**Cu(II)**	**Zn(II)**
Stephylococcus	**Nil**	**10**	**15**	**40**	**15**
Streptococcus	**Nil**	**15**	**15**	**45**	**15**
Bacillus	**Nil**	**11**	**13**	**45**	**20**
E. Coli	**Nil**	**10**	**--**	**50**	**24**
Klebsiella	**Nil**	**9**	**13**	**20**	**20**
Psuedomonas	**Nil**	**8**	**12**	**15**	**15**
DMSO = no activity					

C. DISCUSSIONS

It was observed that all the complexes of AcEE and VEAc showed higher activities than the free ligands. Preliminary antimicrobial studies showed that most of the complexes were active towards all the six bacterial strains and hence a detailed study in this regard will be appreciated.

The results of antibacterial screening tests of the metal complexes of AcEE and VEAc (5mg/ml concentration) are consolidated in **Tables. 5 & 6** and **Fig. 5-8**.

Fig. 5. AcEE complex of Cu(II) (control, 1and 5mg) against *Bacillus*	**Fig. 6. AcEE complex of Fe(III) (control, 1 and 5mg) against *E. Colli***
	

Table. 5: Consolidated antibacterial activities of AcEE and its complexes of concentration 5mg/ml

Si No	**Microorganisms**	**Zone diameter (mm)**				
		AcEE	**Fe(III)**	**Co(II)**	**Ni(II)**	**Cu(II)**
1	***Stephylococcus***	**Nil**	**18**	**16**	**18**	**20**
2	***Streptococcus***	**Nil**	**17**	**15**	**--**	**22**
3	***Bacillus***	**Nil**	**12**	**10**	**15**	**22**
4	***E. Coli***	**Nil**	**15**	**17**	**10**	**18**
5	***Klebsiella***	**Nil**	**15**	**14**	**14**	**15**
6	***Psuedomonas***	**Nil**	**8**	**--**	**10**	**10**

Fig. 7. VEAc complex of Cu(II) (control, 1and 5mg) against *E. Coli.*	**Fig. 8. VEAc complex of Zn(II) (control, 1and 5mg) against *E. Coli.***
	

Table. 6: Consolidated antibacterial activities of VEAc and its complexes, concentration 5mg/ml

Si. No	Microorganisms	Zone diameter (mm)				
		VEAc	Co(II)	Ni(II)	Cu(II)	Zn(II)
1	*Stephylococcus*	Nil	10	15	40	15
2	*Streptococcus*	Nil	15	15	45	15
3	*Bacillus*	Nil	11	13	45	20
4	*E. Coli*	Nil	10	--	50	24
5	*Klebsiella*	Nil	9	13	20	20
6	*Psuedomonas*	Nil	8	12	15	15

Of these AcEE complexes, that of Cu(II) showed higher inhibition than the Fe(III), Co(II) and Ni(II) complexes. However, for the different species of bacteria, these complexes exhibited variation in their activities. The antibacterial activities of the complexes roughly followed the order, Cu(II) > Ni(II) > Fe(III) > Co(II). Thus the metal complexes were found to have higher antibacterial activities than the free ligand, AcEE towards both gram-positive and gram-negative bacteria. (**Table. 5 and Fig. 9-11**)

Fig. 9: Antibacterial activities of the complexes of AcEE, against *staphylococcus* and *streptococus*

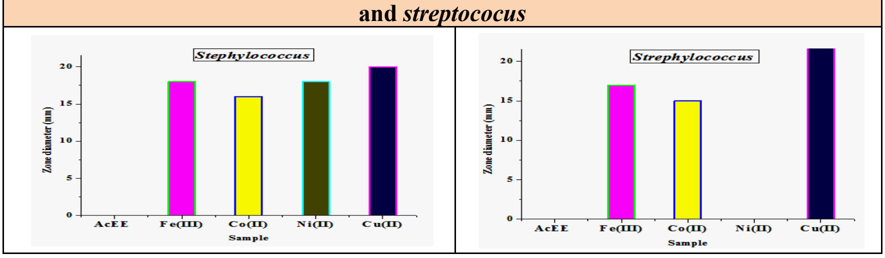


Fig. 10: Antibacterial activities of the complexes of AcEE, against *Bacillus* and *E. coli*

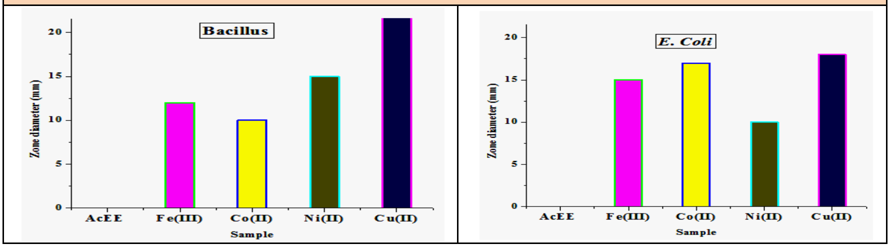
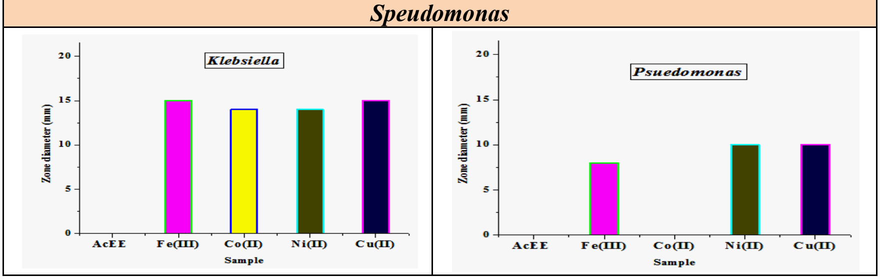


Fig. 11: Antibacterial activities of the complexes of AcEE, against *Klebseilla* and *Speudomonas*



The antibacterial activities of the complexes of VEAc roughly followed the order, Cu(II) > Zn(II) > Ni(III) > Co(II). Thus the metal complexes were found to have better antibacterial activity than the parent ligand, VEAc towards both gram-positive and gram-negative bacteria. (**Table. 6 & Fig. 12-14**)

Fig. 12: Antibacterial activities of the complexes of VEAc, against *staphylococcus* and *streptococus*

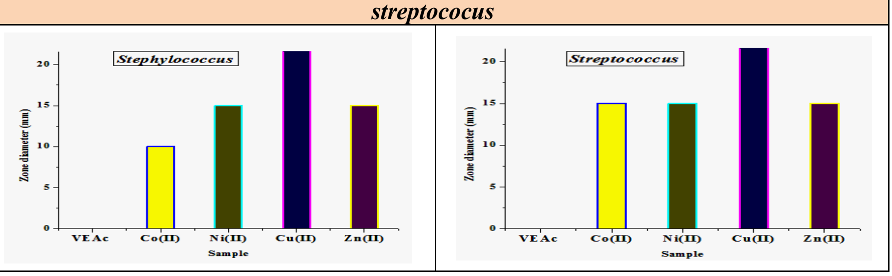


Fig. 13: Antibacterial activities of the complexes of VEAc, against *Bacillus* and *E. coli*

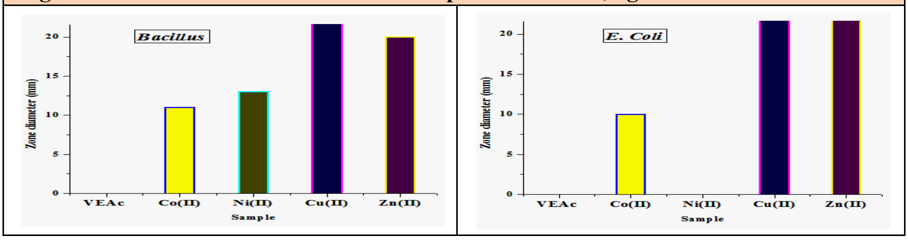
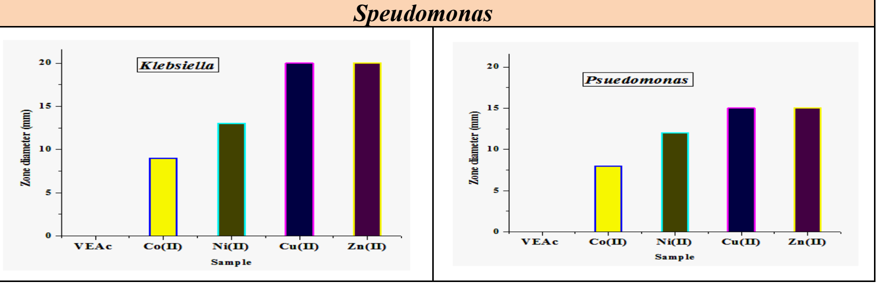


Fig. 14: Antibacterial activities of the complexes of VEAc, against *Klebseilla* and *Speudomonas*



A comparative study of inhibition zone diameter (mg/ml sample) values of the Schiff bases and their metal complexes indicated that the metal complexes exhibited higher antibacterial activities than the free Schiff bases. Such higher activities of the complexes may be explained on the basis of Overtone's concept[19,20] and Tweedy's chelation theory[21,22]. Chelation reduces the polarity of the metal ion significantly because of the partial sharing of its positive charge with the donor atom and also due to pi-electron delocalization on the whole of the chelate ring. Lipids and polysaccharides are some important constituents of the cell walls and- membrane which interact with the metal ions. Apart from this, the cell walls also contain phosphates, carbonyl and cysteinyl ligands which maintain the integrity of the membrane by acting as a diffusion barrier and also provide suitable sites for binding. Furthermore, the decline in polarity increases the lipophilic nature of the chelates and there by the interaction between the metal ion and the lipid is favoured. This may lead to the breakdown of the permeability barrier of the cell, ensuing interference with the normal cell processes.

The Schiff base ligands have modest inhibitory property on the growth of the microorganisms. This is due to the presence of azo-methine groups which have chelating property which may be used in the transport of metal ion across the bacterial membranes or to attach to the bacterial cells at a specific site and interfere with their growth. Therefore, metal complexes show higher bactericidal activities as compared to the free Schiff bases. The present investigation indicated that all of the newly synthesized complexes exhibited different antimicrobial activities. Therefore, it can be concluded that these complexes might be recommended as potential new antibacterial agents[23].

D. CONCLUSIONS

Of the AcEE complexes, that of Cu(II) showed higher inhibition than the Fe(III), Co(II) and Ni(II) complexes. However, for the different species of bacteria, the complexes exhibited variation in their activities in the order, Cu(II) > Ni(II) > Fe(III) > Co(II). The activities of complexes of VEAc roughly followed the order, Cu(II) > Zn(II) > Ni(III) > Co(II). Thus the metal complexes were found to have better antibacterial activity than the parent ligands, AcEE and VEAc. Therefore, it can be concluded that these complexes might be recommended as potential candidates for proper studiesas new antibacterial agents.

Sub-section II

ANTIFUNGAL ACTIVITIES OF THE LIGAND, VEAc AND ITS METAL COMPLEXES

Antifungal screening of VEAc (**Fig. 1**) and its complexes (**Fig. 2**) of Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) was carried out using Disc diffusion or Kirby Bauer method.

Fig. 1. Ligand, VEAc

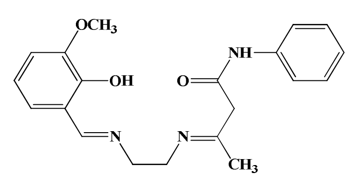
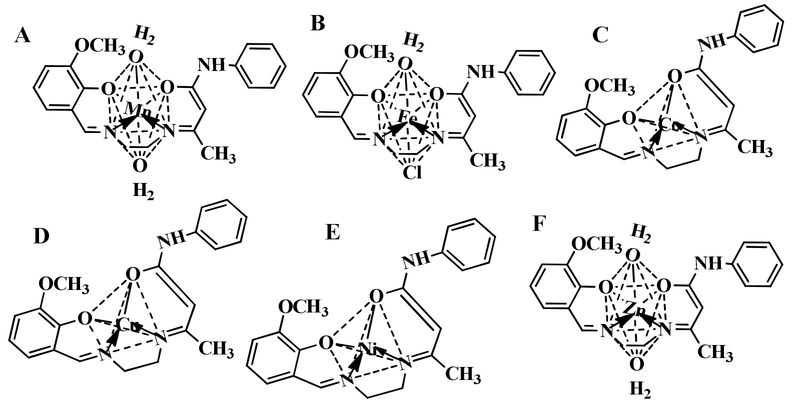


Fig. 4: Structure of Schiff base metal complexes of VEAc: A: Mn(II), B: Fe(III), C: Co(II), D: Ni(II), E: Cu(II) and F: Zn(II)



A. MATERIALS AND METHODS

1. Fungal cultures used

Three fungal cultures, *Pencillium, Fusarium* and *Aspergillus* species were used in the study. The pure cultures were taken from the stock culture maintained in the Microbiology laboratary.

2. Media used

Sabouraud Dexrose Broth

(HiMedia Laboratories Pvt Ltd, Mumbai)

Mycological peptone : 10 g
Dextrose : 40 g
Distilled Water : 1000 ml (p^H – 5.6 ± 0.2)

Sabouraud Dexrose Agar

(HiMedia Laboratories Pvt Ltd, Mumbai)

Mycological peptone : 10 g
Dextrose : 40 g
Agar : 15 g
Distilled Water : 1000 ml (p^H – 5.6 ± 0.2)

3. Evaluation of antifungal activity by Disc diffusion or Kirby Bauer method

Antifungal screening of VEAc and its metal complexes was carried by Disc diffusion method. The fungal cultures were maintained in Sabouraud`s Dextrose broth. From this, 0.1 ml of each culture was uniformly distributed on Sabouraud`s Dextrose Agar (SDA) plates. Sterile filter paper discs of 2 mm diameter were placed on the surface of SDA plates. Drugs of different concentrations, 1 and 5 mg/ml were added on each disc using a micropipette. 2%

DMSO was used as control. The plates were kept at room temperature for two days. After the incubation period, the zone diameters were measured.

B. RESULTS

The antifungal screening was done against the three species, *Pencillinium, Fusarium* and *Aspergillus* by Disc diffusion or Kirby Bauer method. The results are presented in **Table. 1&2** and **Fig. 3 & 4**. VEAc was not found to possess any antifungal activity. However, the complexes showed antifungal activities in a dose dependent manner.

Fig. 3. Complex of Cu(II) (control, 1and 5mg) against *Pencillinium* and *Aspergillus*

Table.1. Antifungal activity of VEAc and its complexes, Conc. 1mg/ml

Species	Zone diameter (mm)						
	VEAc	**Mn(II)**	**Fe(III)**	**Co(II)**	**Ni(II)**	**Cu(II)**	**Zn(II)**
Pencillinium	**Nil**	**8**	**7**	**11**	**10**	**14**	**10**
Fusarium	**Nil**	**8**	**Nil**	**8**	**11**	**15**	**7**
Aspergillus	**Nil**	**5**	**6**	**9**	**7**	**13**	**9**

Fig. 4. Complex of Cu (II) and Zn(II) (Control, 1 and 5mg) against *Fusarium*

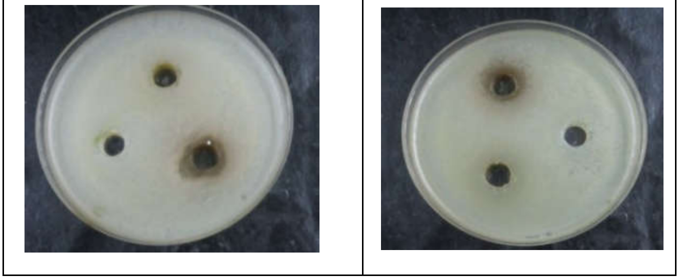


Table.2. Antifungal activity of VEAc and its complexes, Conc. 5mg/ml

Species	Zone diameter (mm)						
	VEAc	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Zn(II)
Pencillinium	Nil	11	12	12	14	26	18
Fusarium	Nil	10	Nil	14	17	25	20
Aspergillus	Nil	Nil	9	11	11	20	17

C. DISCUSSIONS

The antifungal screening of VEAc and its complexes showed that the metal complexes were more potent than the parent ligand. The studies revealed that all the metal complexes were active towards the fungal stains in a concentration dependent manner[19]. From the studies, Ni(II), Cu(II) and Zn(II) complexes were found to have higher activity [Cu(II) > Zn(II) Ni(II)] both at 1mg/ml and 5mg/ml concentration, while Mn(II), Fe(III) and Co(II) complexes exhibited lower activity. (**Fig. 5-8**)

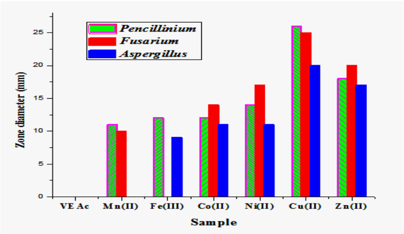
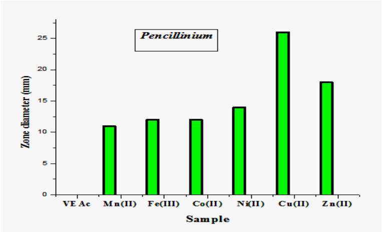
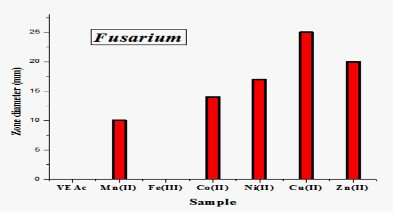
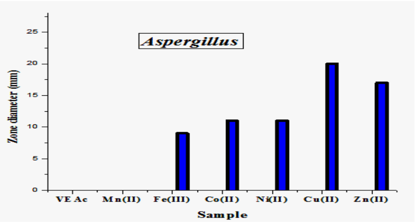
Fig. 5. Consolidated antifungal activities of VEAc and its complexes	Fig. 6: Antifungal activity of VEAc and its complexes against *Pencillinium*
	

Fig. 7: Antifungal activity of VEAc and its complexes against *Fusarium*	Fig. 8: Antifungal activity of VEAc and its complexes against *Aspergillus*
	

The higher activities of the metal complexes than the free ligand may be explained on the basis of Overtone’s concept [20,21] and Tweed`s Chelation theory[22,23]. According to Overtone`s concept of cell permeability, the lipids membrane that surrounds the cell favours the passage of lipids soluble materials alone, due to which liposolubility is an important factor which controls the biological activities of the drugs. On chelation, the polarity of the central metal ion will be decreased to a considerable extent due to the overlap of the ligands orbitals and the partial sharing of the positive charges of the metal ions with the donor groups. Further, it increases the delocalisation of л-electrons over the whole chelating ring and enhances the lipophilicity of the metal complexes. This enhanced lipophilicity enables the penetration of the complexes into lipid membranes and blocks the metal binding sites in the enzymes of the organisms[24]. These complexes may also perturb the respiration process of the cell and thus block the protein synthesis, resulting in the interference with the normal cell division process[24].

D. CONCLUSIONS

The investigation on the antifungal activities showed that the Ni(II), Cu(II) and Zn(II) complexes were found to have higher activity [Cu(II) > Zn(II) Ni(II)], while Mn(II), Fe(III) and Co(II) complexes exhibited lower activity. The data obtained showed that the complexes exhibited higher antifungal activity as compared to the control (blank) and the ligand.

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Chapter X

CYTOTOXIC AND ANTITUMOR STUDIES OF THE LIGAND, VEAc AND ITS METAL COMPLEXES

A. INTRODUCTION

In the present scenario, cancer is one of the prominent health risks for humanity[1]. Regardless of the dramatic growth of antitumour drugs, cancer death rate remains constant. *Cis*-platin is the significant platinum based anticancer drug[2] used against numerous human cancers, chiefly in bladder-, testicular-, head-, ovarian- and neck cancers[3,4]. However, structural analogues of *cis*-platin have not yet overcome its clinical demerits, mainly with regard to a dose limiting toxicity, nephrotoxicity, neurotoxicity, ototoxicity, nausea and the lower activity in some of the most familiar cancers[5]. In order to surmount rigorous side effects, numerous platinum-based complexes, like *carbo*-platin and *oxali*-platin have been used in the cancer treatment[6,7]. In addition, there are some other Pt anticancer drugs, like *neda*-platin, *pico*-platin or redox-active Pt(IV)-based *satra*-platin, *tetra*-platin, and *orma*-platin[8]. Literature survey showed that the transition metal complexes of Schiff bases show antitumor property[9-24].

1. Antitumor properties of Schiff base metal complexes

In the last few decades, several other metal complexes, such as those of Ru, Cu, Co and V have received much attention as potential anticancer agents[25-36]. The anticancer activity of Schiff base complexes in mammalian cells is by inhibiting ribonucleotide reductase, an essential enzyme in the synthesis of DNA precursors[37]. Iron and copper complexes are shown to be more active in the inhibition of DNA synthesis than the free ligand[38]. Earlier studies showed that the

Cu(II) complex of 2-formylpyridine thiosemicarbazone was very powerful antitumor agent than the free ligand[39].

Abd El-Halim *et.al*[40] prepared a new Schiff base ligand by the condensation of quinoline-2 carboxaldehyde with 2-aminophenol and its complexes with a series of transition metal ions, Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II) and Cd(II). In addition, the Schiff base ligand and its mixed ligand metal complexes were tested against breast cancer cell line (MCF-7) and colon cancer cell line (HCT-116). The results against breast cancer cell line (MCF-7) showed that all metal complexes have IC50 higher than the free ligand. The compounds can arranged as follows in the decreasing order of their activities Cd(II) > Cu(II) > Zn(II) > Ni(II) Co(II) > Mn(II) Cr(III) > Fe(III) > 2, 2`-bipy. The results against colon cancer cell line (HCT-116) showed that all metal complexes have IC50 higher than free ligand and complexes can be arranged in the decreasing order of their activities as follows, Cd(II) > Zn(II) > Cu(II) > Ni(II) > Mn(II) > Co(II) > Cr(III) > Fe(III)2 > 2, 2`-bipy.

Khalil *et.al*[41] reported novel binuclear curcumin complexes of Cu, Zn and Cd. These complexes showed cytotoxic activity. It was suggested that the size of the coordinated metal ions might play a significant role in determining the cytotoxic activity of these complexes by blocking the central carbon atom with the labile hydrogen.

A series of novel water-soluble Pt(II) complexes of Schiff bases were synthesized by Li-Jun Li *et.al*[42]. These compounds were screened for their interaction with salmon sperm DNA. Their *in vitro* anticancer actions have been estimated against HL-60, KB, BGC-823, and Bel-7402 cell lines by the MTT assay. The cytotoxicity of one of these complexes was better than that of *cis*-platin against BGC-823 and HL-60 cell lines and showed comparable cytotoxic effect against Bel-7402 cell line.

Mahmoud *et.al*[43] reported a novel Schiff base ligand, 2,20-((1-Z,10-Z)-(1,3-phenylene *bis*(azanylylidene)) *bis*(phenylmethylylidene))dibenzoic acid, obtained by the condensation of *m*-phenylenediamine with *o*-benzoylbenzoic acid. Anticancer properties of the ligand and its metal complexes were evaluated. The Cd(II) complex showed higher anticancer properties than the others with IC_{50} 9l g/mL in the clinical trials.

Some novel Cu(II) complexes of the Schiff bases, obtained by condensation of 2-[N-(a-picolyl)-amino] benzophenone with different amino acids, were synthesized by Yang *et.al*[44]. The cytotoxicities of the complexes were estimated against human cancer cells. The cytotoxicities of the complexes depended on the substituents on the aromatic ring. Complexes with ligands having bromine as a substituent on the pyridine rings showed higher cytotoxicity. The screening against tumour cell lines was assayed *in vitro* and the complexes were found to be highly effective. It was noted that the six of the nine complexes had better activity than that of the ligand.

Raja *et.al*[45] synthesized some novel Ru(III) complexes of the Schiff base derived from 4-aminoantipyrine and substituted salicylaldehyde. The cytotoxicity of the free ligand and $[RuCl_2(AsPh_3)L]$ were slightly lower than the standard anticancer drug, *cis*-platin.

A new Schiff base ligand derived from 3-formylchromone and benzohydrazide and its Ni(II), Zn(II), Ru(II), Ru(III), Pd(II), Pt(II) and Ag(I) complexes were synthesized by Elsayed *et.al*[46] . The ligand and its metal complexes have been tested as anticancer agents against the human breast cancer (MDAMB231)- and human ovarian cancer (OVCAR-8) cell lines and Ag(I) complex showed the good efficacy.

Three novel transition metal complexes, $[ML_2(phen)]\cdot H_2O$ (M= Mn, Co or Zn; HL = $C_{10}H_7NSe$, 2-phenyl-4-selenazole carboxylic acid and phen = 1, 10-phenanthroline) were prepared by Yin *et.al*[47]. The anticancer action of the complexes against human pancreatic cancer line, PANC-28 and human hepatocarcinoma line, HuH7 was evaluated. The interactions between DNA and these compounds were studied by using ethidium bromide (EB) fluorescent probe.

A new ligand, *N*-Nicotinoyl-*N*-*o*-hydroxythiobenzhydrazide (H_2Notbh) and its complexes, [Mn(Notbh)(H_2O)] and [M(Notbh)], where, M=Ni(II), Cu(II) or Zn(II) were reported by Srivastav *et.al*[48] . All the complexes inhibited the growth of tumour, whereas the ligand did not. *In vivo* administration of these metal complexes resulted in persistence of survival of tumour bearing mice. Tumour bearing mice administered with these metal complexes showed reversal of tumour growth and associated induction of apoptosis in lymphocytes.

Binuclear Cu(II) and Mn(II) complexes of the 5-benzylidene-3-(4-chlorophenyl)-6-oxo-5,6-dihydro-1-*H*-[1,2,4]-triazine-2-carbothioic acid amide (HL1) and 5-(3-bromo-4-methoxybenzylidene)-3-(4-chloro-phenyl)-6-oxo-5,6-dihydro-1-*H*-[1,2,4]-triazine-2-carbothioic acid amide (HL2) have been synthesized by Refat *et.al*[49]. Inhibitory activities against breast carcinoma cells (MCF-7 cell line), hepatocellular carcinoma cells (HePG-2 cell line) and colon carcinoma cells (HCT cell line) were evaluated by using various concentrations of the samples (50, 25, 12.5, 6.25, 3.125, and 1.56 μg) and cell viability (%) was determined by colorimetric method. The Cu(II) complex of HL1 was found to be active against MCF-7, HEPG-2 and HCT cell line.

B. SCOPE OF THE PRESENT INVESTIGATION

Petering[50] reported that the Cu(II) ion itself has no antitumor activity, but will act as an inhibitor of tumour growth in the chelated or complexed form. Even though the exact pathway by which copper chelates reduce cancer growth is not known, it is supposed that this will be on the basis of structure activity relationship, as in the case of *cis*-platin[51] (i.e. DNA intercalation). The review also exposed that Schiff bases of diamine were extensively studied, but not many, which showed considerable biological activities.

Schiff bases ligand, o-vanilline-(1,2-ethylenediimine)acetoacetanilide (VEAc) derived from vanillin and acetoacetanilide with 1, 2-ethylenediamine and their transition metal complexes were studied here. The tetradentate (N2O2) Schiff base, VEAc and its Cr(III), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) complexes were investigated for their *in vitro* cytotoxicity and antitumour activity.

C. EXPERIMENTAL

1. Synthesis

The detailed procedures for the synthesis of the ligand, VEAc (**Fig. 1**) and its Cr(III), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) complexes (**Fig. 2**) are discussed in **Chapter. V**

Fig. 1: Structure of the ligand, VEAc (L2H)

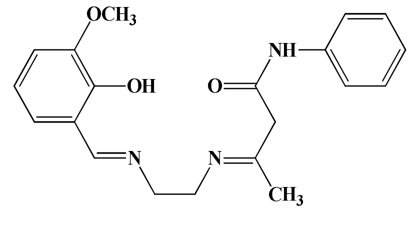
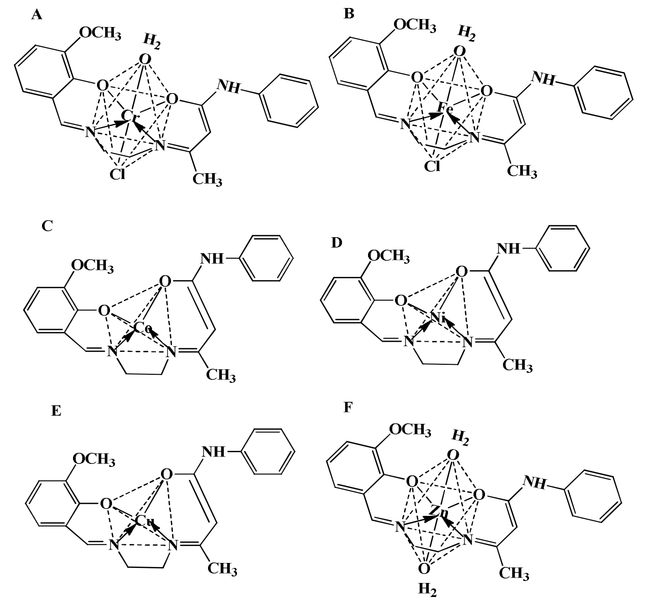


Fig. 2: Structure of Schiff base metal complexes. A: Cr(III), B: Fe(III), C: Co(II), D: Ni(II), E: Cu(II) and F : Zn(II)



D. ANTICANCER STUDIES

1. Preparation of the drug and its evaluation of anticancer potential

For *in vitro* studies, 50 mg of the compound (VEAc) was dissolved in 1 ml of dimethylsulphoxide (DMSO) was used. For *in vivo* studies, this solution was further diluted using distilled water to the desired concentration.

Adayar Cancer Institute, Chennai provided essential Ehrlich Ascites Carcinoma (EAC) cell lines and Dalton's Lymphoma Ascites (DLA) cell line and were propagated as transplantable tumours in the peritoneal cavity of BALB/C mice. L929 (mouse lung fibro blast) cell line was obtained from National Centre for Cell Sciences, Pune.

The experiments were carried out on laboratory Swiss albino female mice (20-25 g) and were obtained from the Small Animal Breeding Station, Mannuthy, Thrissur, Kerala and they were kept under standard conditions of temperature and humidity in animal house of Amala Cancer Research Centre, Trissur, Kerala. The animals were fed with standard mouse chow (Sai Durga Feeds and Foods, Bangalore, India) and water *ad libitum*. All the animal experiments in this study were carried out with the prior approval of the Institutional Animal Ethics Committee (IAEC) and were conducted strictly according to the guidelines of CPCSEA constituted by the Animal Welfare Division, Government of India.

Dalton's Lymphona Ascites (DLA) and Ehrlich's Ascites Carcinoma (EAC) cells maintained in the intraperitoneal cavity of mouse were used for the study.

2. Trypan Blue exclusion method

The test compounds were studied for short-term *in vitro* cytotoxicity using Dalton's lymphoma ascites cells (DLA). The tumour cells aspirated from the peritoneal cavity of tumour bearing mice were washed thrice with PBS or normal saline. Cell viability was determined by Trypan Blue exclusion method[52].

3. Toxicity studies of Cu(II) complex

24 Swiss albino mice were divided (6 animals) into 4 groups (group- 1, 2, 3 and 4). 5, 10, 15 and 20 mg/kg of drug was administrated once daily (Intraperitoneal Injection) to the group 1, 2, 3 and 4, respectively, and continued for 5-6 weeks to determine their mortality rate. (**Fig. 1**)

Fig. 1: Normal Swiss albino mice

4. Use of Cu(II) complexes for the treatment of mice bearing acites

a. On the survival rate of ascites tumour bearing mice

Based on the toxicity studies of Cu(II) complex, mice (female, 6–8 weeks old) weighing 26–30 g were divided into 5 groups of 6 animals each. Viable EAC cells 106 in 0.1 ml of phosphate buffered saline (PBS) were injected in to the peritoneal cavity of the mice. Group 1 was used as control. Groups 2, 3 and 4 were injected, respectively, with 5, 10 and 15 mg/Kg of the prepared drug [Cu(II) complex]. Gram 5 was administrated with the standard drug (Cyclophosphamide)

Drug and cyclophosphamide were given by intraperitoneal injection from the first day of tumour induction. The death pattern of animals due to tumour burden was noted and the percentage of increase in life span was calculated as, % ILS= (T-C/C) ×100, where T and C are mean survival of treated and control mice, respectively.

b. On solid tumour development

Swiss albino mice (6 - 8 weeks old) weighing 23–28 g were splitted into five groups, each group composed of 6 animals. DLA cells (0.1 ml of 106 cells per mouse) were administrated by injection in to the right hind leg of mice to induce tumour growth. Group 1 was used as control animals. Copper complex of VEAc was given to the 2nd, 3rd and 4th groups for treatment. Group 5 was taken as standard animals and injected standard drug, cyclophosphamide. The tumour growth on the mice of each group was arbitrated by estimating the diameter of tumour volume in two perpendicular planes using a digital vernier calliper, starting from 7th day of tumour growth up to 31st day. The volume of tumour development was calculated using the equation, $V=4/3\pi r_1^2 r_2$, where r_1 is the minor diameter and r_2 is the major diameter[25].

E. RESULTS

1. Short-term *in vitro* cytotoxic analysis

The Schiff base ligand, VEAc and its Cr(III), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) complexes exhibited striking cytotoxic activity for DLA cell line (Table 1). The copper complex showed highest activity and the concentration required for 50% death (IC_{50}) was found to be 47 µg/ml.(**Table. 2** & **Fig. 3-10**)

Table. 2: Percentage of cytotoxicity of ligand, VEE and its complexes

Concentration (µg/ml)	Percentage of Cytotoxicity						
	Complexes						VEAc
	Cr(III)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Zn(II)	
200	52	70	71	57	84	72	36
100	43	52	51	45	71	59	26
50	31	43	44	32	56	41	16
20	20	36	32	23	29	36	12
10	10	31	25	13	22	24	7

Fig. 3: Cytotoxic action of ligand and its complexes

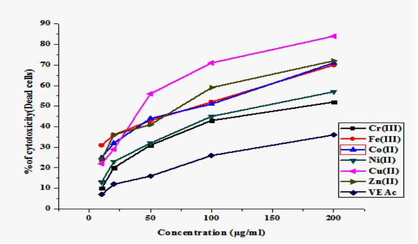


Fig. 4: Cytotoxic action of ligand

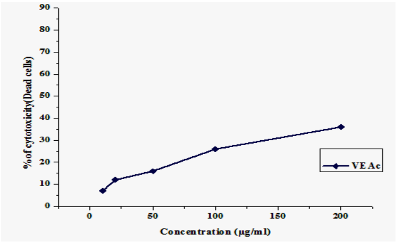


Fig. 5: Cytotoxic action of ligand and its Cr(III) complex

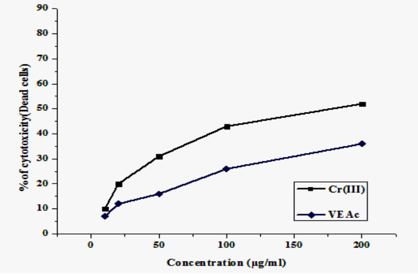


Fig. 6: Cytotoxic action of ligand and its Fe(III) complex

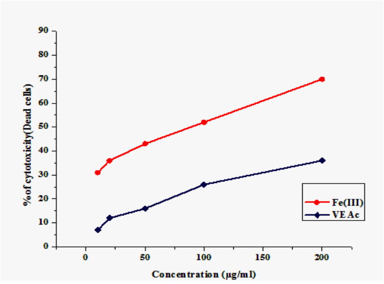


Fig. 7: Cytotoxic action of ligand and its Co(II) complex

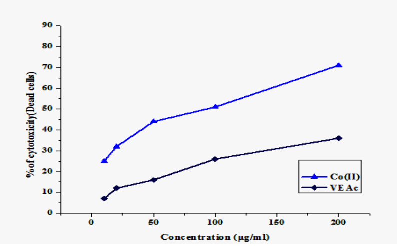


Fig. 8: Cytotoxic action of ligand and its Ni(II) complex

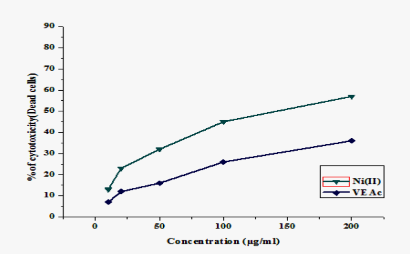


Fig. 9: Cytotoxic action of ligand and its Cu(II) complex

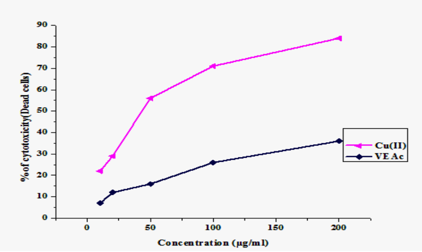
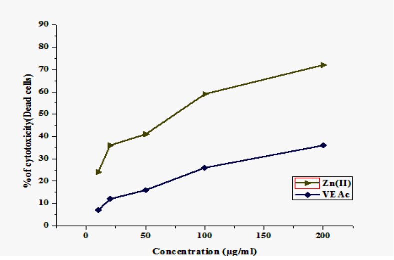


Fig. 10: Cytotoxic action of ligand and its Zn(II) complex



2. Toxicity studies of the drug

The results of toxicity studies of the copper complex on 24 Swiss albino mice, 4 groups, at four concentrations (20, 15, 10 and 5 mg/kg) showed that 20 mg/kg was slightly toxic to the animals. Therefore, that concentration was avoided and 15, 10 and 5 mg/kg were selected for *in vivo* studies, as they were nontoxic to the animals.

3. Effect of copper complex on ascites tumour development

The animals in the tumour control group survived for a period of 15.2 days. Those treated with cyclophosphamide survived for 25.8 days. The copper complex at 15, 10 and 5 mg/kg increased the survival rate of the animals by 18.6, 19.6 and 22 days, respectively. (Showned in **Table. 2 & Fig. 11)** Thus the copper complex was found to be effective in increasing the average life span of the animals by 44.7, 29 and 22.3 %, respectively, at 5, 10 and 15 mg/kg doses (**Fig. 12-16**).

Table. 2: Effect of Cu(II) complex on survival rate of ascitis tumour enduring mice

Treatment (mg/kg)	Survival rate (Days)
Control	15.2
15	18.6
10	19.6
05	22
Standard*	25.8

*cyclophosphamide (10)

Fig. 11: Effect of Cu(II) complex on survival rate of ascitis tumour enduring mice

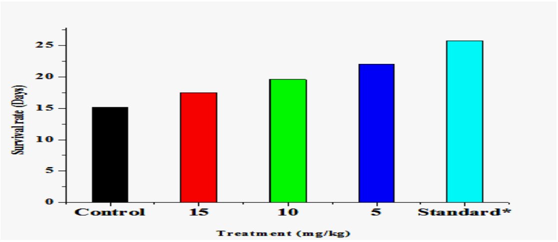


Table. 3: Effect of copper complex of VEAc on the life span rate of ascitis tumour enduring mice

Treatment (mg/kg)	Increase in Life span (%)
Control	--
15	22.3
10	29
05	44.7
Standard*	69.7

* cyclophosphamide (10)

Fig. 12: Effect of Cu(II) complex on survival rate of ascitis tumour enduring mice

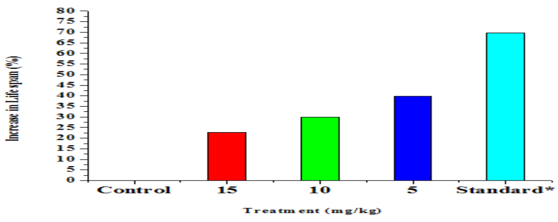


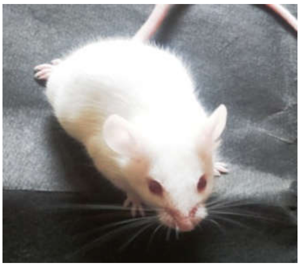
Fig. 13. Ascites tumour bearing mice 1st day	**Fig. 14. Ascites tumour bearing mice 5th day (5mg/kg)**
	

Fig. 15. Ascites tumour bearing mice 10th day (5mg/kg)	**Fig. 16. Ascites tumour bearing mice 20th day (5mg/kg)**
	

4. Effect of copper complex on reduction of solid tumour volume

Tumour volume of the animals in the control group enlarged by 3.001 cm^3 on 31th day, while in the case of animals treated with the Cu(II) complex, there was a significant decrease of tumour volume. At 5 mg/kg, the volume was 1.429 cm^3, while at higher concentrations (15 and 10 mg/kg) the tumour volumes were found to be 1.844 and 1.742 cm^3, respectively. In the case of the animals treated with standard drug, cyclophosphamide, the reduction in tumour volume was 0.698 cm^3 (**Table 4 & Fig. 17-20)**

Table 4: Effect of copper complex of VEAc on the reduction of tumour volume (cm^3)

Dosage (mg/kg)	Observation (No: of days)								
	Initial	10th	13th	16th	19th	22nd	25th	28th	31st
	*Tumor volume (cm^3)								
Control	0.094	0.701	0.990	1.421	1.982	2.341	2.681	2.994	3.001
15	0.080	0.510	0.591	0.682	0.834	0.884	0.992	1.120	1.844
10	0.079	0.423	0.423	0.794	0.844	0.923	1.024	1.342	1.742
05	0.078	0.484	0.484	0.642	0.714	0.794	0.948	1.012	1.429
Standard	0.080	0.214	0.214	0.248	0.304	0.400	0.490	0.514	0.698

*Mean volume in cm^3

Fig. 17: Standard group (solid tumour bearing mice)	Fig. 18: Copper complex treated 10 mg/Kg
	

Figure. 19: Effect of copper complex of VEAc on solid tumour induced by Dalton`s lymphoma ascites cells.

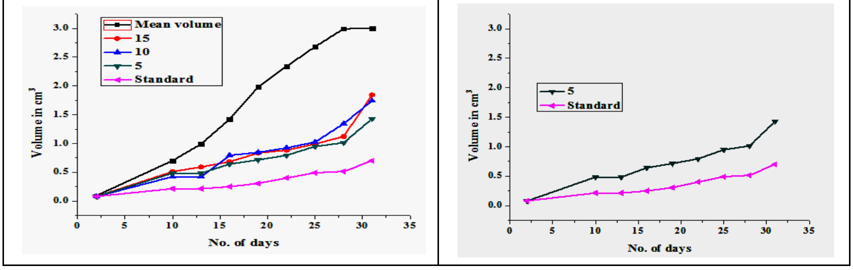
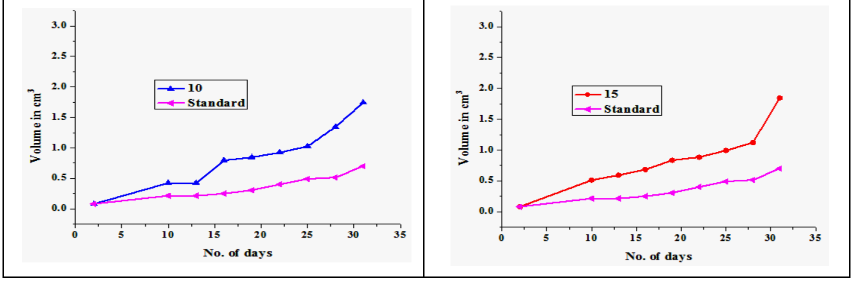


Figure. 20: Effect of copper complex of VEAc on solid tumour induced by Dalton`s lymphoma ascites cells.



F. DISCUSSIONS

The antitumour studies of o-vanillin-(1,2-ethylenediimine) ethylacetoacetate (VEAc) and its Cr(III), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) complexes yielded interesting and promising results. This is common feature for all compounds containing N-N-S and O-N-O donor atom. *In-vitro* cytotoxicity studies on VEAc and its metal complexes showed cytotoxicity against DLA cell lines. The copper complex showed highest cytotoxicity with an IC_{50} value of 47µg/ml.

From the present studies, we have concluded that the copper complex of VEAc is efficient against EAC-induced ascites tumour. A concentration of 5 mg/kg body weight was more effective than the other two concentrations (15 and 10 mg/kg b.wt). The *in vitro* cytotoxic studies of the copper complex suggested its potential use as an anticancer agent.

G. CONCLUSIONS

In the present study, a Schiff base ligand, *o*-vanilline-(1,2-ethylenediimine)-*o*-hydroxyacetophenone (VEAc) and its Cr(III), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) complexes have been synthesized and evaluated their antitumour activities. *In vitro* cytotoxicity studies of the ligand, VEAc and its complexes showed activity against DLA cell lines. The copper complex showed highest cytotoxicity with an IC_{50} value of 47 μg/ml. From the present study, we concluded that the copper complex of VEAc was effective against EAC-induced ascites and DLA-induced solid tumour. *In vitro* cytotoxic studies of the Cu(II) VEAc complex suggested its potential use as an anticancer agent.

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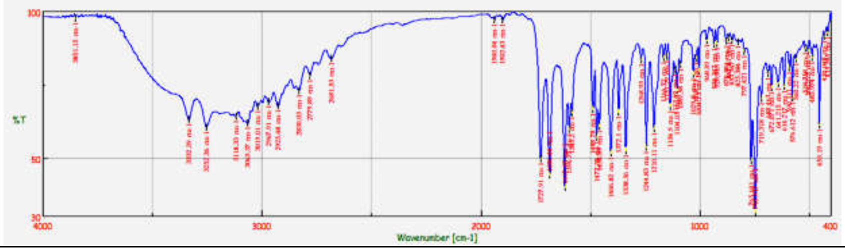
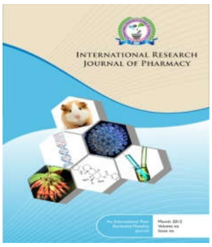
APPENDIX-I

Fig. 4a: IR spectrum of Cr(III) complex



Publications

	Subin kuamr. K, Priya Varma C, Reena VN, Aravindakshan. K K, Synthesis, Characterization, Cytotoxic, Anticancer and Antimicrobial Studies of Novel Schiff Base Ligand Derived From *o*-Vanillin and Its Transition Metal Complexes, ***Journal of Pharmaceutical Sciences and Research***. 9(8), 1317-1323 (**2017)**
	Subin Kumar. K, Aravindakshan. KK, Synthesis, Characterization Antimicrobial and Antioxidant Studies of Complexes of Fe(III), Ni(Ii) and Cu(II) with Novel Schiff Base Ligand (E)-Ethyl 3-((3-Aminopropyl)Imino)Butanoate, ***Journal of Pharmaceutical Chemical & Biological Sciences***. 5(3), 177-186 (**2017)**
	Subin Kumar. K, Aravindakshan K. K, Antitumor, Cytotoxic And Antimicrobial Studies Of A Novel Schiff Base, *ortho*-Vanillin-(1,2 Ethylenediimine) *ortho*-Hydroxyacetophenone And Its Transition Metal Complexes, ***Journal of Pharmaceutical Chemical & Biological Sciences***. 5 (3), 271-281 (**2017)**
	Subin Kumar. K, Priya Varma. C, Reena. V. N, Aravindakshan. K. K, Cytotoxic, antitumor and antimicrobial studies of a oxygen and nitrogen donor, novel schiff base ligand, acetoacetanilide-(1, 2-ethylenediimine)ethylacetoacetate and its first series transition metal complexes, ***International Research Journal of Pharmacy***, 8(10), 160-166 (**2017)**