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REVIEW

Amino Acid Based Schiff Bases and Their Metal Complexes as Biologically Potent Agents

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Schiff bases derived from amino acids and their corresponding metal complexes have been widely studied in different ways and have increased attention of chemists in biological, pharmaceutical and biochemical fields due to their easy synthesis and broad spectrum of applications. In this review, we have focused on the synthesis and biological evaluation involving antifungal, antibacterial, anticancer, antioxidant and antidiabetic activities of some amino acid derived Schiff bases and their respective metal complexes.

Keywords: Amino acid, Schiff base, Metal complexes, Biological evaluation.

INTRODUCTION

There is considerably increasing interest for the synthesis of metallic complexes due to their versatile coordination behaviour and acceptance ability of molecules practice [1,2]. The adaptability of these Schiff base ligands and chemical, analytical, biological and pharmacological suitability of their complexes generate the need of further explorations in this field [3,4].

Schiff bases and their biological significance: Organic compounds having an azomethine group (-CH=N-) known as Schiff base. Schiff base product was innovated by German chemist Hugo Schiff [5]. Schiff base ligands are very important in branch of coordination chemistry, since Schiff base formed potentially stable when coordinate to metal ions [6]. Schiff bases are generally easy to synthesize, derivate and have good ligation power. Schiff bases are usually synthesized by condensation of aldehydic or ketonic group with primary amine group containing compound [7]. Schiff bases are very stable and can change the ligation characteristic by altering the basicity and denticity [8]. Schiff bases usually act as bidentate or tridentate ligands with different donor sites *i.e.* N, O or S responsible for formation of stable complexes with different transition metals. There is chemical, biological and medicinal importance of Schiff base because of the presence of imine nitrogen of azomethine [9-11] linkage (-CH=N-) with an unshared pair of electrons present in the sp^2 hybridized orbital. Schiff bases show a wide range of biological activities that include anti-microbial [12-15], anticancer [16-22], anti-inflammatory [23-27], anticonvulsive [28,29], antiretroviral [30], anti-HIV [31] and antipyretic [32] activities.

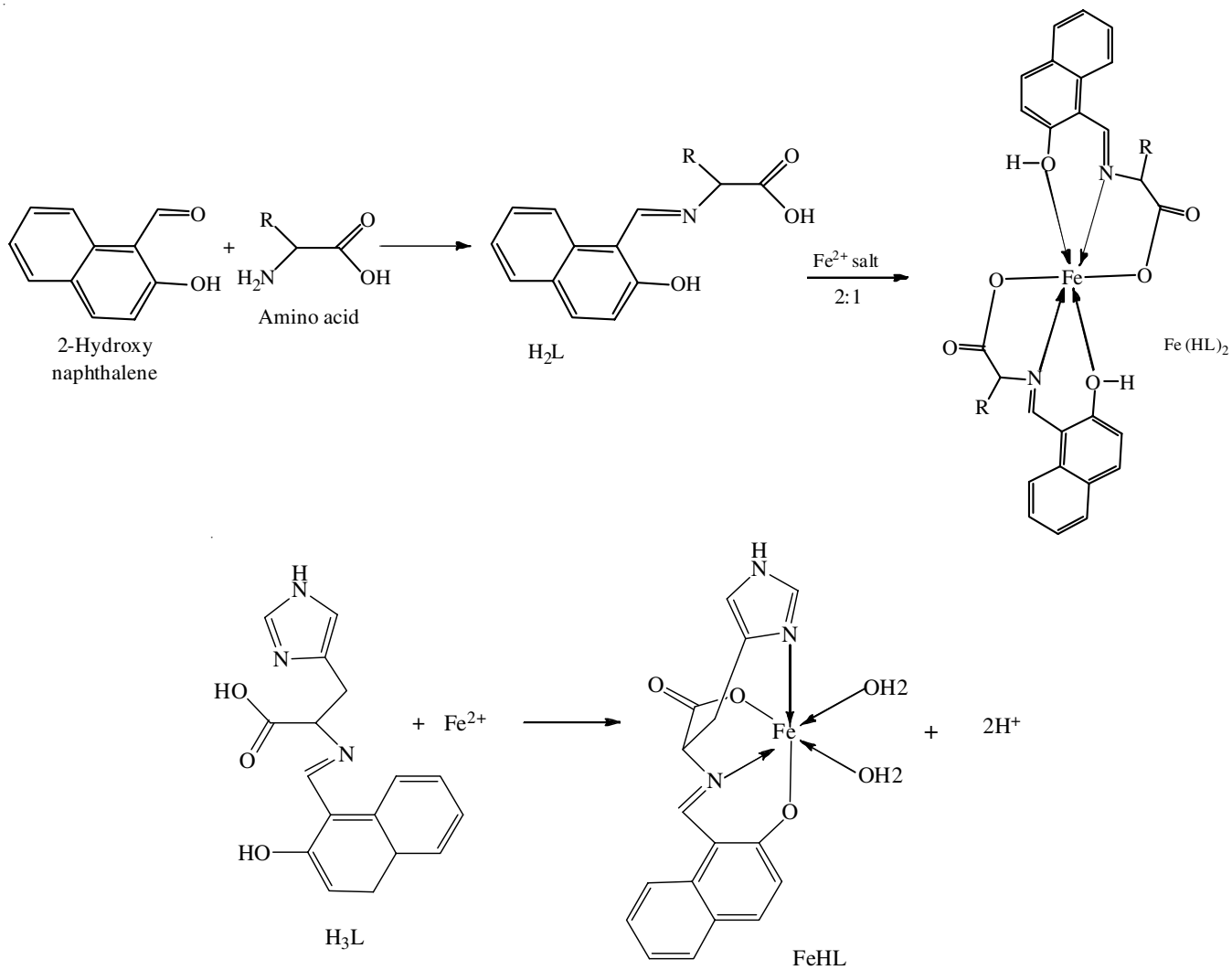
Amino acid based Schiff base: Amino acids are acidic, basic or neutral molecules that comprise a carboxylic acid group at α-position, an amine group and a side chain that varies from one to another amino acid [33-37]. These are generally significant in biochemistry [38-40]. Amino acids generally have the formula H_2N-CH(R)-COOH, where R, is an organic moiety. The amino acid Schiff base ligands can be prepared by condensation reaction of carbonyl compound with the amine group containing amino acid [41-43]. In above synthetic process of amino acid and aldehyde group, pH plays an important role and mostly base (NaOH/KOH) is required for completion of reaction [44,45]. In amino acid Schiff base synthesis, amino acids are specifically very effective chelating ligands, which act as easily available chiral bioactive predecessor and efficient and better-targeted drug moieties [46-50]. These amino acid Schiff base ligands typically can act as bidentate or tridentate coordinated through N donor atom of imine group (-CH=N-) and O^- ion of carboxylate (COO^-) functional groups [51]. These types of ligands also exhibit variable denticity towards metal ions.

Specific metal based complexes and their importance: Amino acid Schiff base generates thermally and chemically stable metal complexes [52-55] with many transition metal ions such as V, Fe, Mn, Co, Ni, Cu, Zn, Zr, Pb *etc.* Some Schiff bases of amino acids and their metal complexes with Zr(IV), Pb(II) have been synthesized by Singh & Singh [56,57]. Al-Shaheen *et al.* [58] prepared amino acid Schiff bases and iron(III) metal complexes. Some researchers have also synthesized several selective metal complexes of lanthanides [59-62]. The amino acid Schiff bases and their metal complexes account for constituting novel potent antibacterial and anticancer reagents and many of them reported to exhibit antifungal, antidiabetic, antioxidant and larvicidal activity [60-89]. In recent years, Schiff base ligands and their corresponding metal complexes which contain sulphur have gained more attention in medicinal chemistry [90-95]. Amino acid Schiff bases complexes have received importance from the inorganic and biochemistry aspects and due to their pharmacological and physiological activities [96-101].

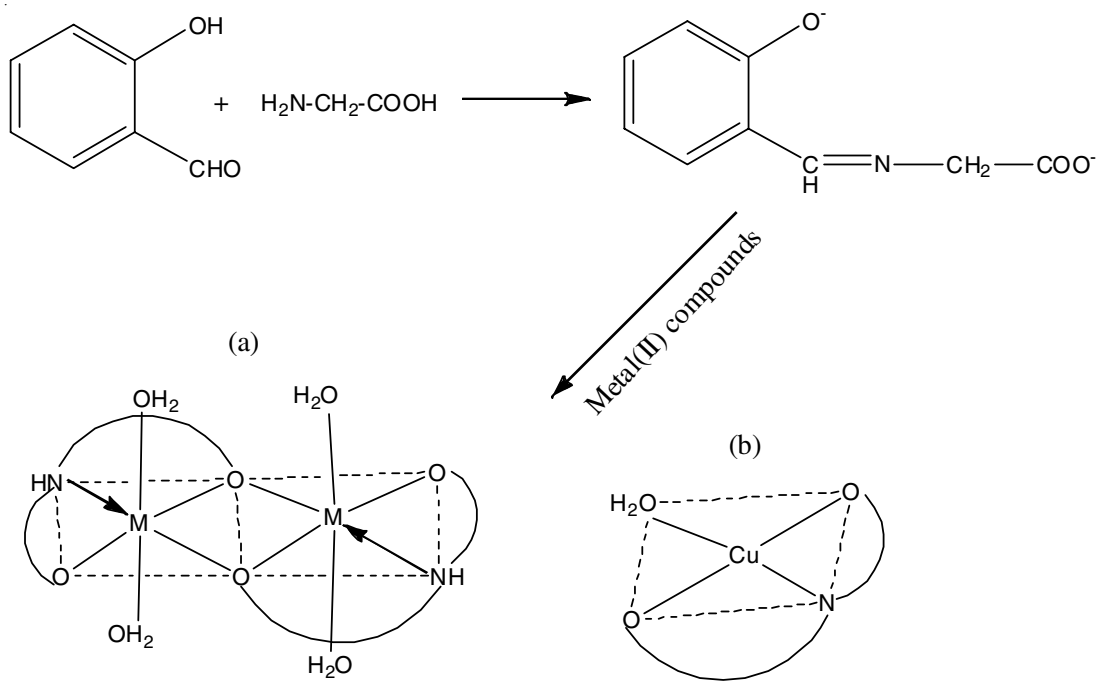
Synthesis and biological studies: Accordingly, research studies on the molecular structure and physico-chemical properties of Schiff based metal complexes have provided interesting new results. So, there is a need to survey and compare with earlier literature. This review compiles biological significance of amino acid derived Schiff bases and their corresponding metal complexes.

Antimicrobial activity: Abdel-Rahman *et al.* [60] prepared some novel Fe(II) Schiff base amino acid complexes $[Fe(HL)_2]$ and $[FeL(H_2O)_2]\cdot 2H_2O$ that are derived from the synthesized Schiff base ligands H_2L and H_3L (**Scheme-I**). All the newly prepared ligands and synthesized metal complexes were found to exhibit remarkable antibacterial and antifungal activity. These are screened against selective bacterial strains *B. cereus*, *E. coli* and *P. aeruginosa* and selective fungal strains, *A. flavus P. purpurogenium* and *T. rosium* employing the disc diffusion method to evaluate their antimicrobial potential. This study demonstrated marked enhancement in biological activity when coordinates with the metal ions. This increased potency can be explained by virtue of extra azomethine linkage formed by ligand.

Islam *et al.* [61] synthesized new Schiff base complexes which are derived from 2-hydroxybenzaldehyde and glycine with some transition metals (**Scheme-II**). All the complexes have screened against selective bacterial strains like as *E. coli, S. sonnei*, *S. lutea*, *S. aureus*, *P. aeruginosa* and *B. subtilis* to



Scheme-I: Synthesis of amino acid Schiff base ligands and their iron complexes



Scheme-II: Synthetic route for Schiff base and its metal complexes {(a) dimeric O_h for M = Ni(II), Co(II) and Zn(II) (b) Cu(II) square planer complex}

measure their antibacterial activities by disc diffusion method. Results showed that the potency of Cu complex was good against all the bacteria strains followed by Ni, Co and Zn complexes with moderate activity.

Lanthanide(III) {La^{3+}, Gd^{3+}, Nd^{3+}, Sm^{3+} and Ce^{4+} metal ions} complexes and the Schiff base ligand (H_3L) (Figs. 1 and 2) have been synthesized by Alghool *et al.* [62]. The biological activity of the ligand and its metal complexes was measured against various bacterial and fungal pathogens. The synthesized compounds have been screened against *S. aureus* (Gram-positive bacteria), *E. coli* (Gram-negative bacteria) and two fungal strains *C. albicans* and *A. flavus*. But ligand showed more activity rather than the metal complexes.

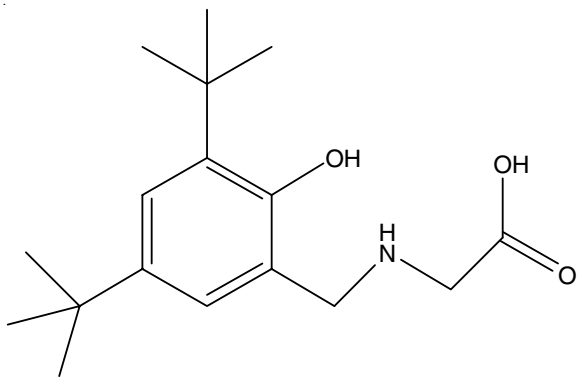
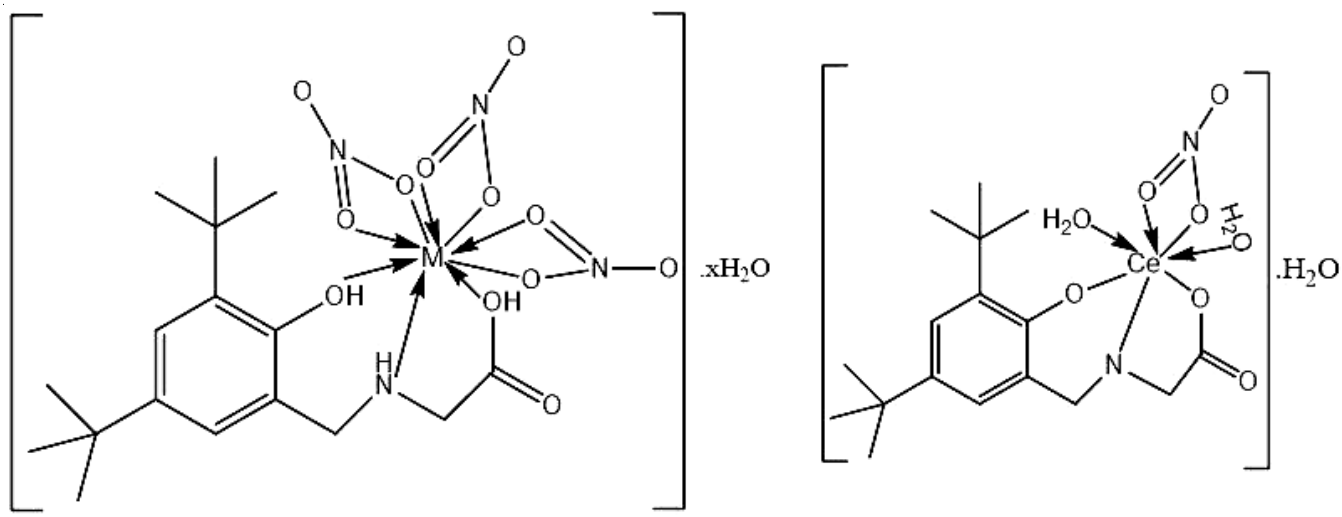


Fig. 1. Proposed structure of H_3L where H_3L = [(3,5-di-*tert*-butyl-2-hydroxybenzyl)amino]acetic acid



where M = La(III), Gd(III), Nd(III), Sm(III), x = 1, 2, 3

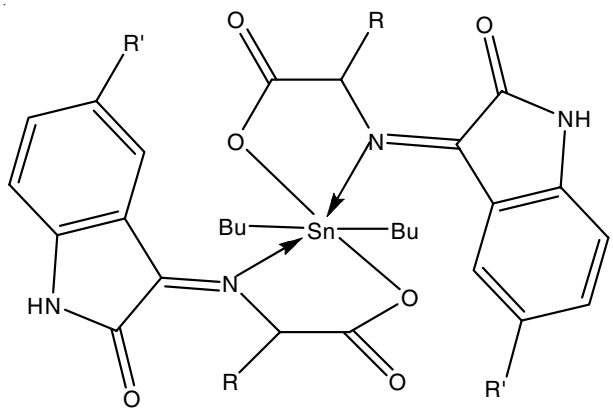
Fig. 2. Proposed structure of the metal(III) complexes

The amino acid Schiff bases have been synthesized by the condensation reaction of benzaldehyde or acetone with phenylalanine amino acid, respectively (L_1, L_2) in presence of NaOH as a catalyst and their corresponding complexes have been synthesized by Al-Jaboori *et al.* [63] The antibacterial activity of synthesized complexes of copper and cobalt of L_1 have been evaluated against two pathogenic bacteria *S. aureus* and *E. coli*. It was found that the complexes show significant antibacterial activity with former, not with later.

Sachdeva *et al.* [64] synthesized the Schiff bases from isatin derivatives, selected amino acids and thiosemicarbazide in an aqueous medium by an environment benign green process (**Scheme-III**). The newly synthesized compounds have been found biologically active against some tested pathogens. Later, these were evaluated against *A. niger*, *P. notatum, F. oxysporum, A. brassicicola*, *etc.* for antifungal activity and *S. aureus, B. licheniformis* and *M. luteus* (Gram-positive bacteria) and *E. coli* and *P. aeruginosa* and (Gram-negative bacteria) for antibacterial activity. It was clear from the results that all the synthesized compounds have higher antibacterial activity than the antifungal activity.

Singh & Singh [65] reported the design and synthesis of some new-fangled tin complexes formulated as $[Bu_2Sn(L)_2]$ (Fig. 3) and amino acid Schiff bases prepared from some α-amino acids and isatin derivatives (**Scheme-IV**). These synthesized compounds have been screened for antibacterial activities against selective bacterial strains like *S. saprophyticus*, *B. cereus* (Gram-positive bacteria) and *Klebsiella* spp., *E. coli* (Gram-negative bacteria). This study demonstrated that the metal complexes exhibit significant and enhanced antibacterial activity against certain microbial strains as compared to the free ligands.

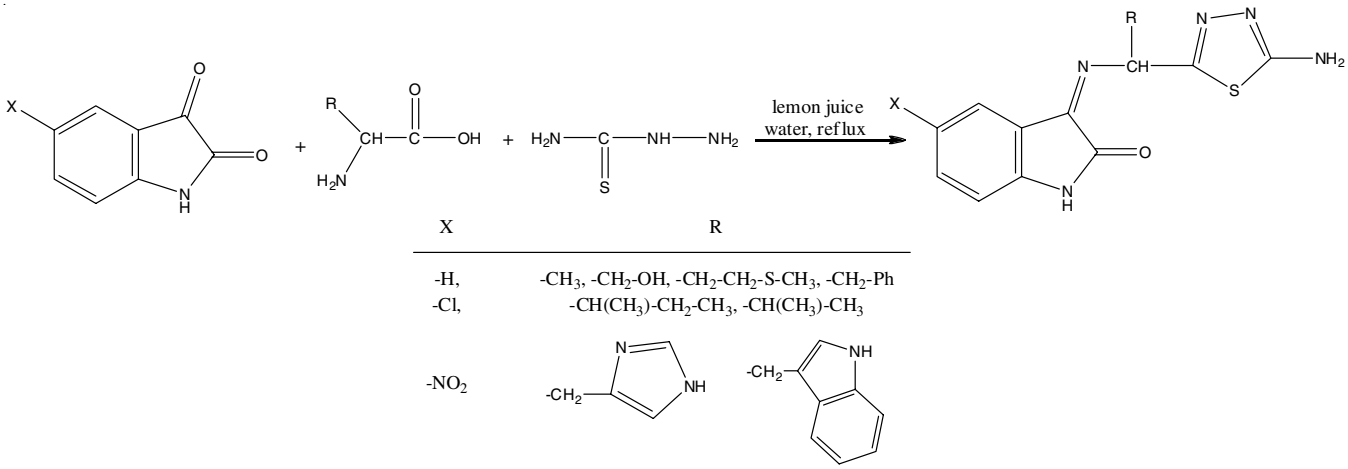
Abbas [66] has synthesized a novel mono azo Schiff base ligand, (2-(4-aminoantipyren)-L-tryptophane) (AAT), acted as bidentate with O, N- donor sites (**Scheme-V**). Metal complexes formulated as $[Ln(AAT)_2Cl_3]$ of this synthesized ligand have been prepared by coordination with Ln(III) chloride salts (Fig. 4). Antimicrobial activities of all the newly synthesized compounds have been evaluated against two bacterial strains *S. aureus* and *E. coli* and two fungal pathogens *A. niger* and *C. albicans* employing the diffusion technique. It has been concluded that metal complexes after chelation with ligands showed greater antimicrobial activity as compared to free ligand.



where, R = -CH_2-Ph, $CH(CH_3)$ C_2H_5, -H; R′ = -H, -Cl

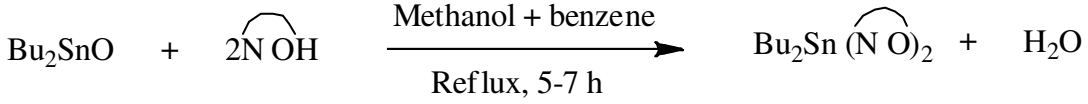
Fig. 3. Structure of $[Bu_2Sn(L)_2]$ complex

Some new-fangled binuclear metal complexes $[M_2L(AcO)_2(H_2O)_4]$ (Fig. 5) have been derived from substituted 1,3-dioxapropane (L) and L-tryptophan by Ciolan *et al.* [67]. The antimicrobial properties of all the synthesized complexes have been evaluated against some bacterial pathogens; *S. aureus*, *S. epidermidis*, *Bacillus* sp. (Gram-positive bacteria), *Salmonella* sp., *P. aeruginosa*, *K. pneumoniae* (Gram-negative bacteria) and also one fungal strain *C. albicans* by spot method for quali-



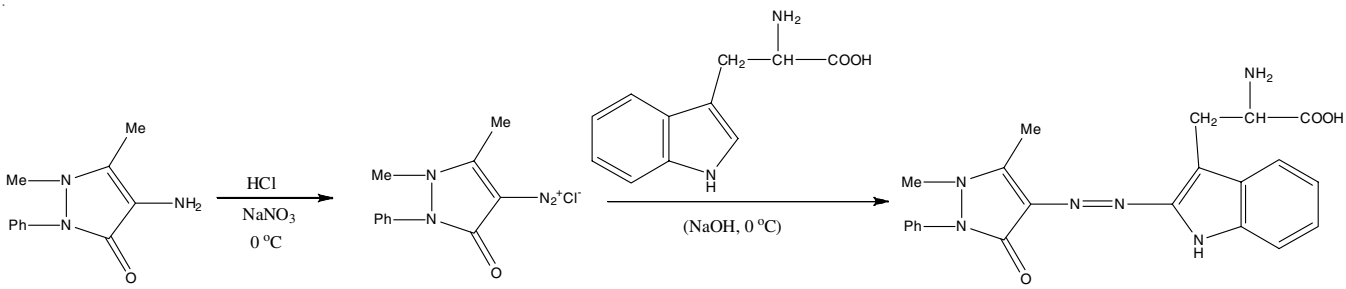
X	R
-H,	-CH_3, -CH_2-OH, -CH_2-CH_2-S-CH_3, -CH_2-Ph
-Cl,	-$CH(CH_3)$-CH_2-CH_3, -$CH(CH_3)$-CH_3
-NO_2	

Scheme-III: Proposed synthetic route for Schiff bases



where, $\overset{\frown}{N\,OH}$ presents the donor sites of Schiff bases

Scheme-IV: Proposed equation for the synthesis of dibutyltin(IV) complexes



Scheme-V: Preparation of ligand (AAT)

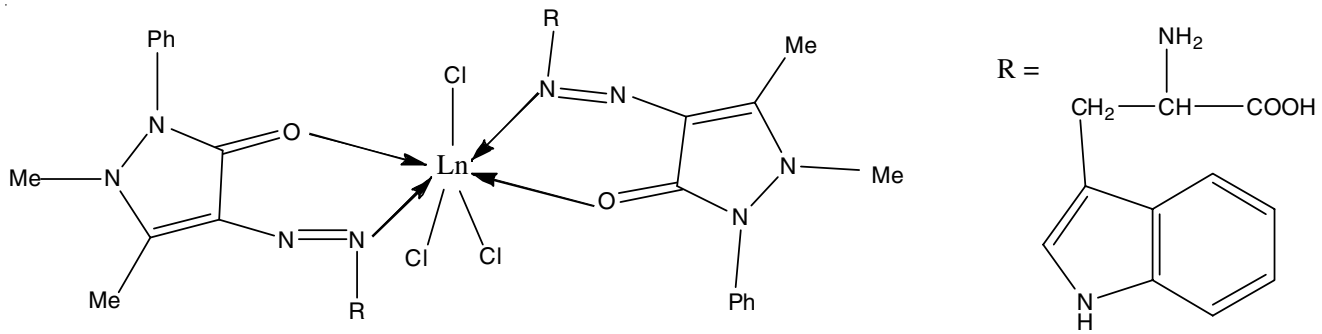


Fig. 4. Proposed structure of the synthesized metal complexes

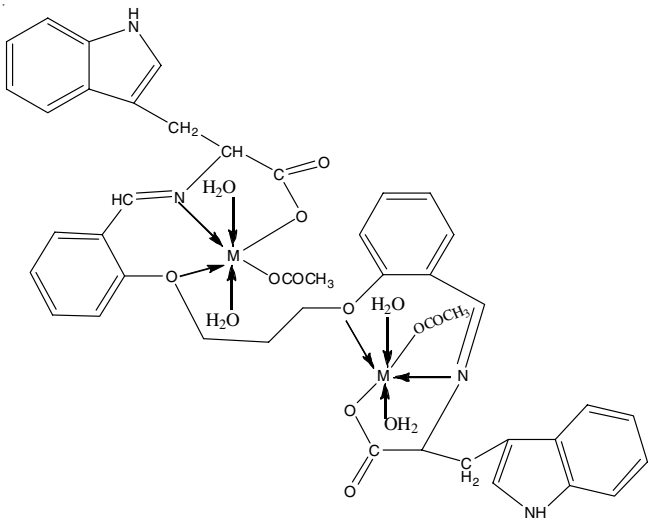


Fig. 5. Structure of the synthesized metal complexes

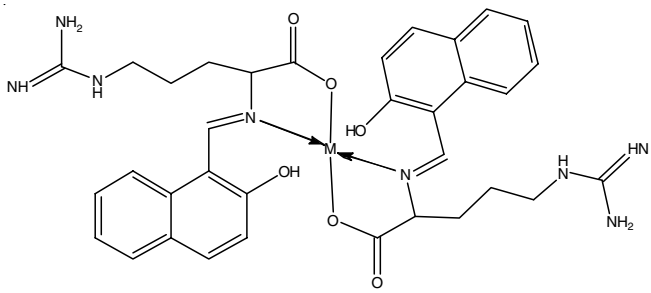
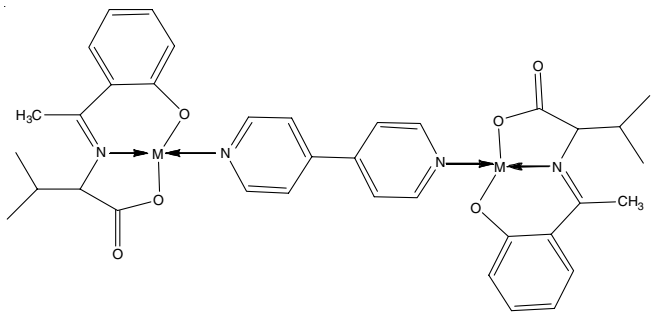


Fig. 6. Structure of amino acid Schiff base metal complexes



where M = Ni(II), Co(II), Zn(II), Cu(II) and Cd(II); L_2 = 4,4'-bipyridyl

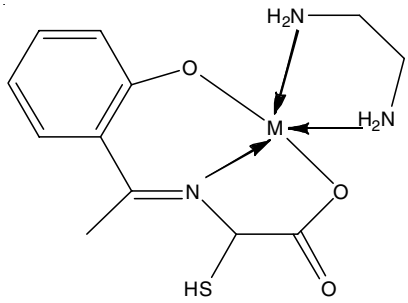
Fig. 7. Proposed structure for synthesized metal complexes

tative screening and binary micro dilution method for quantitative screening. The complexes are found to follow: Cu(II) > Mn(II) ≈ Co(II) > Ni(II) order for antimicrobial activity and Copper complexes also showed remarkable activity against *S. marcescens* strain.

Novel Schiff base ligand LAHN has been synthesized and further used for complexation with Co(II), Mn(II) and Zn(II) metal salts (Fig. 6) as reported by Iniama *et al.* [68]. Both complexes and ligand demonstrated a remarkable antimicrobial properties against *S. aureus*, *E. coli*, *S. typhi* and *C. albicans* strains have been examined *in vitro* by disc diffusion method. The metal complexes having a higher inhibition activities comparison to the free ligand.

Some novel Schiff base ligand (L_1) and their corresponding transition metal complexes formulated as [ML_1L_2] (Fig. 7) have been synthesized by Saranya *et al.* [69]. Both ligand and the synthesized complexes have been studied for antimicrobial properties against selective bacterial strains *P. aeruginosa, S. aureus, Bacillus* sp. and *E. coli* and fungal pathogens *Rhizopus* sp., *A. flavus* and *Mucor* sp. Almost all the complexes were found to exhibit significant potency against certain microbes compared to the Schiff base ligand. Cobalt(II) and cadmium(II) complexes were found to possess good antibacterial activity against *S. aureus*.

In continuation of this work, new-fangled Schiff base ligand (L_1) formed by the reaction of *o*-hydroxyacetophenone with L-cysteine and its transition metal complexes of the type $[ML_1L_2]$ (Fig. 8) (L_2 = ethylenediamine) have been synthesized [70]. The antimicrobial studies of all the newly synthesized complexes and respective ligand have been screened against some bacterial strains like *S. aureus*, *E. coli*, *K. pneumoniae*, *P. aeruginosa* and fungal strains like *A. niger*, *A. flavus* and *P. notatum*. The larvicidal activity of the synthesized complexes follow the order; $[CuL_1L_2] > [ZnL_1L_2] > [NiL_1L_2] > [MnL_1L_2] = [CoL_1L_2]$. In addition, Zn(II) complex also show antioxidant activity.



Where M = Mn(II), Ni(II), Co(II), Cu(II) and Zn(II)

Fig. 8. Proposed structure of the metal complexes

Some novel complexes of Ag(I), Cu(II) and Au(III) in which MBP employed as ligand act as bidentate where N(azo) and N′(imidazole) are donor atoms, have been synthesized by Abbas & Khadim [71]. The molar ratio of M:L in Cu(II) and Ag(I) complexes obtained was 1:2 except 1:1 molar ratio in Au(III) complex. Both ligand and synthesized complexes were found to show better antibacterial activity towards bacteria strains *E. coli* and *S. aureus*. General formula of all the synthesized complexes were as $[Cu(MBP)_2Cl_2]$, $[Ag(MBP)_2]NO_3$, $[Au(MBP)Cl_2]Cl$ (Fig. 9).

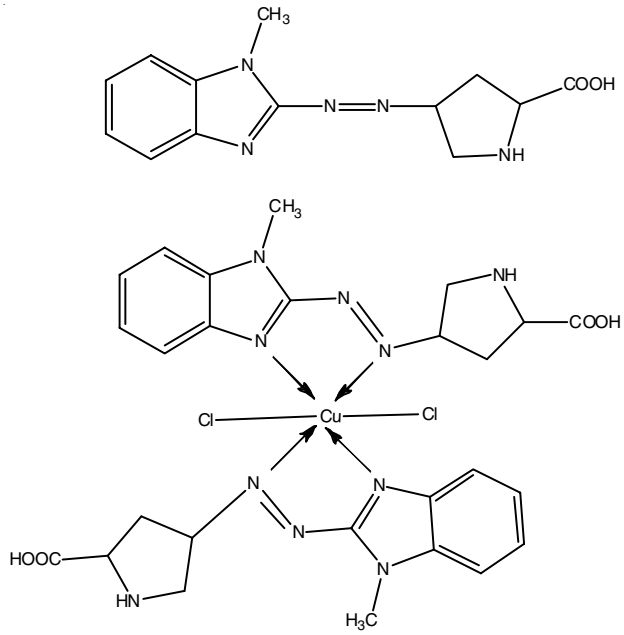
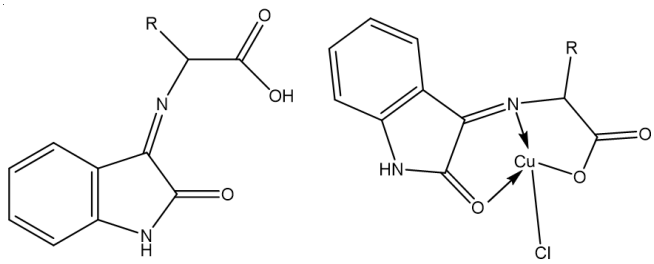


Fig. 9. Structure of MBP ligand and its Cu(II) complex

Anatony *et al.* [72] synthesized Schiff base amino acid derived from glycine, alanine, salicylaldehyde and benzoic acid derivative and its Zn(II) complexes. Antimicrobial studies revealed the effect of complexation which may be confirmed by the result that Schiff base ligands do not show positive antibacterial activity when screened against *E. coli*. Later glycine salicylaldehyde Schiff base Zn(II) complex exhibit higher antimicrobial activity in comparison to other two, showing the maximum affinity of Schiff base ligands to Zn(II) ion.

Schiff base ligands of 1*H*-indole-2,3-dione with some amino acids have been synthesized and used for the synthesis of Cu(II) complex [73]. The antimicrobial activity of Schiff bases and its Cu(II) complex (Fig. 10) have been evaluated by using the disc diffusion method. The complexes were found to exhibit strong inhibitory action against *S. aureus*, *B. subtilis*, *P. vulgaris* and *E. coli*. The Cu(II) complex showed maximum inhibition activity against *S. aureus*.



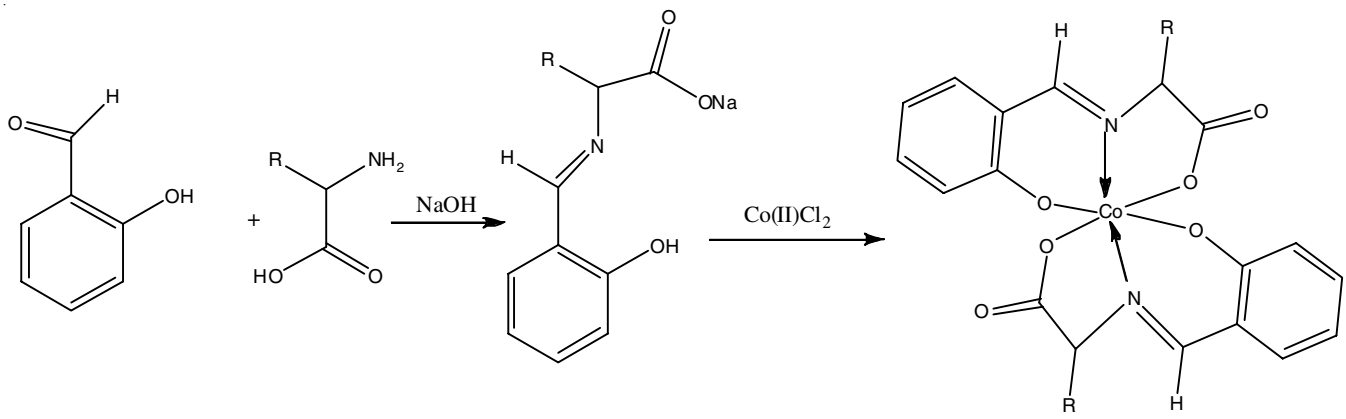
where R = CH_2SH, CH_3, $CH_2CH(CH_3)_2$, H

Fig. 10. General structure of amino acid Schiff base and its metal complex

Salama *et al.* [74] reported the synthesis and characterization of Co(II) complexes based on amino acid Schiff base and the Schiff bases were synthesized from salicylaldehyde and some selective amino acid in a medium of base (**Scheme-VI**). All the free ligands have antibacterial activity against these bacteria *B. subtilis* and *S. aureus* (Gram-positive bacteria) and *E. coli* and *P. aeruginosa* (Gram-negative bacteria). Their Co(II) complexes showed greater antibacterial activity when screened against most of the bacterial and fungal strains (*C. albicans*). But none of the ligands showed any activity against *C. albicans* and *A. flavus* fungi.

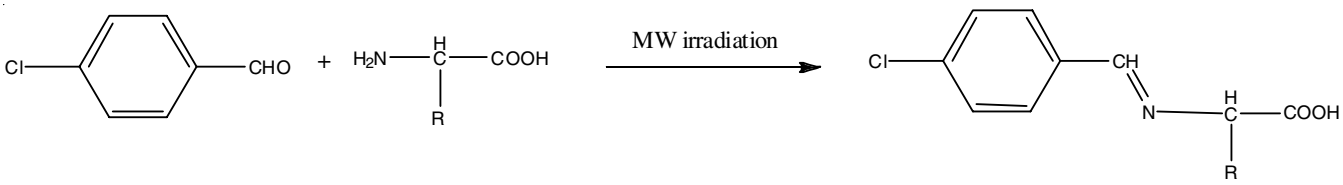
Al-Salami *et al.* [75] synthesized various Schiff base ligands derived from *p*-chlorobenzaldehyde with some selective amino acid using a microwave assisted process (**Scheme-VII**). All the synthesized Schiff base ligands and their metal complexes (Fig. 11) were tested to examine their bacterial activity against both Gram-positive bacteria *S. aureus* and Gram-negative bacteria *A. hydrophile*. It was also concluded that the complexes have higher and better antibacterial activity as compared to free Schiff base ligand. This enhanced activity was described according to lipid existing in cell membrane and the solubility and penetration power of complexes in lipid.

A novel Schiff base derived from L-arginine and benzaldehyde was synthesized and further used for complexation with some metal ions to form Schiff base complexes (Fig. 12) [76]. All the newly synthesized compounds were assayed against *S. aureus*, *A. niger*, *E. coli*, *P. mirabilis*, *C. albicans*, *etc.* It

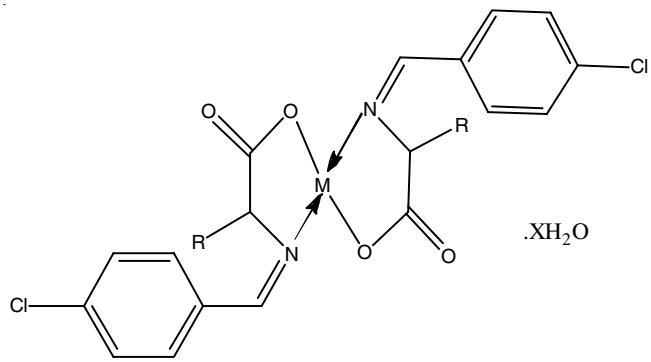


where R = $CH(CH_3)$, $CH_2CH(CH_3)_2$, CH_2CH_3, $CH(CH_3)_2$

Scheme-VI: Chemical equation for the synthesis of AA Schiff base ligand and its complex

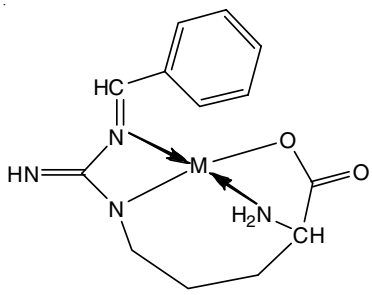


Scheme-VII: Schematic reaction of Schiff base synthesis



where R = CH_3, $CH(CH_3)_2$, Ph-CH_2 X= 1, 2, or 3
M = Zn(II), Ni(II), Cd(II), Cu(II) or Co(III)

Fig. 11. General proposed structure of synthesized metal complex



where M = Ni(II), Fe(II) and Co(II)

Fig. 12. Proposed structure of amino acid Schiff base metal(II) complexes

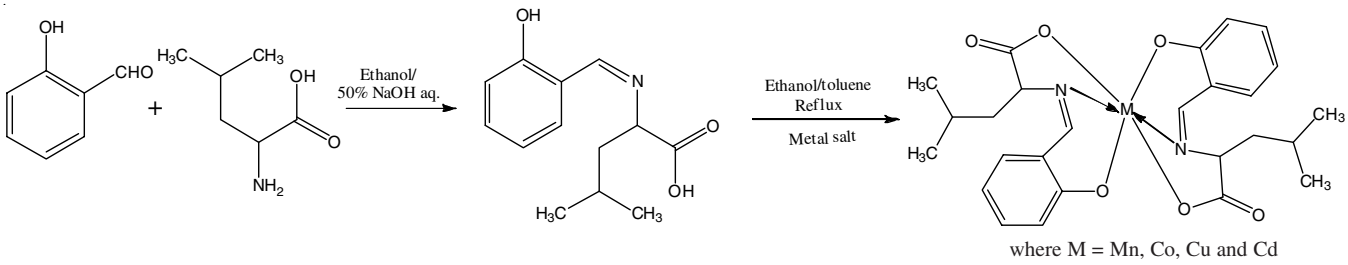
was concluded that the synthesized complexes are biologically more active in comparison to the Schiff base ligand.

Pervaiz *et al.* [77] synthesized novel amino acid based Schiff base and used for the synthesis of Mn, Co, Cu and Cd complexes in presence of base (**Scheme-VIII**). The antimicrobial studies demonstrated that the metal complexes exhibit remarkable antibacterial and antifungal activities than the parent ligand. The inhibitory action checked against various bacterial strains *i.e. S. aureus*, *B. sabtilus* and *E. coli* and fungal strains *i.e. A. niger*, *A. flavus* and *A. alternata*.

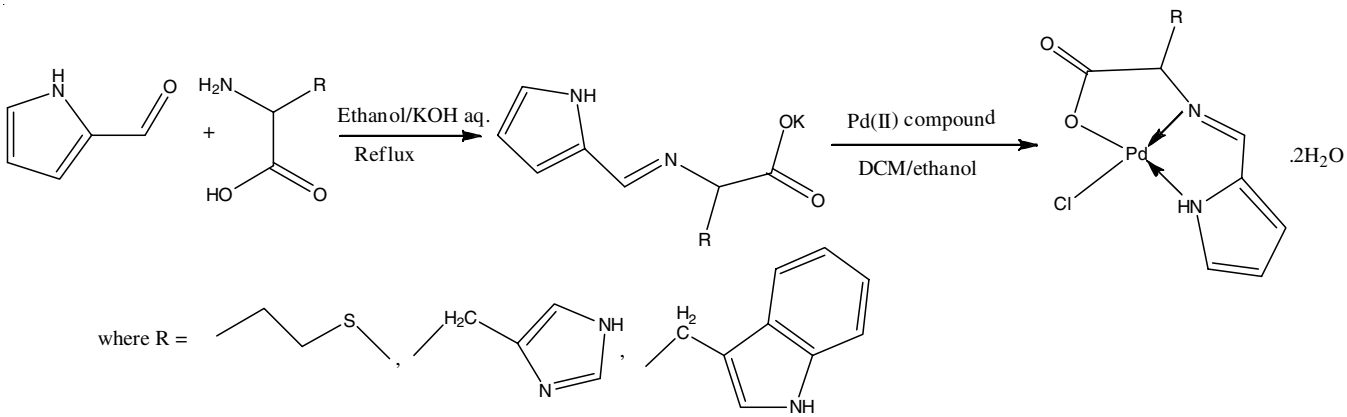
The Schiff base ligands named as L_1, L_2 and L_3 were obtained by condensation reaction of pyrrole-2-carboxaldehyde with different amino acids methionine, histidine and tryptophan, respectively. These Schiff bases further employed for complexation with palladium(II) to form Schiff base complexes C1, C2 and C3 (**Scheme-IX**) [78]. The antibacterial activity of all synthesized compounds have been examined against various bacteria *S. epidermidis*, *P. aeruginosa*, *S. pyogenes*, *K. pneumonia*, *etc.* The aliphatic sulphur group containing complex C1 showed lower influence on bacteria, whereas other complexes C2 and C3 having heterocyclic ring (imidazole and indole ring) found to exhibit the highest antibacterial activity at the lowest concentrations.

Some new amino acid Schiff bases have been synthesized from 3-methoxysalicyaldehyde or 4-diethylaminosalicylaldehyde with selective amino acids. Further, complexation of these ligands carried with Cu metal salt as reported by Rehman *et al.* [79]. All the synthesized compounds screened for antimicrobial activity and found that the metal complex have greater antibacterial and antifungal activity rather than Schiff base ligands. The above synthesized complex and ligands screened against some bacteria pathogens like *B. sabtilus*, *E. coli* and *M. luteus* to check their antibacterial activity and some fungi pathogens like *A. niger, C. glabrata* and *S. cerevisiae*.

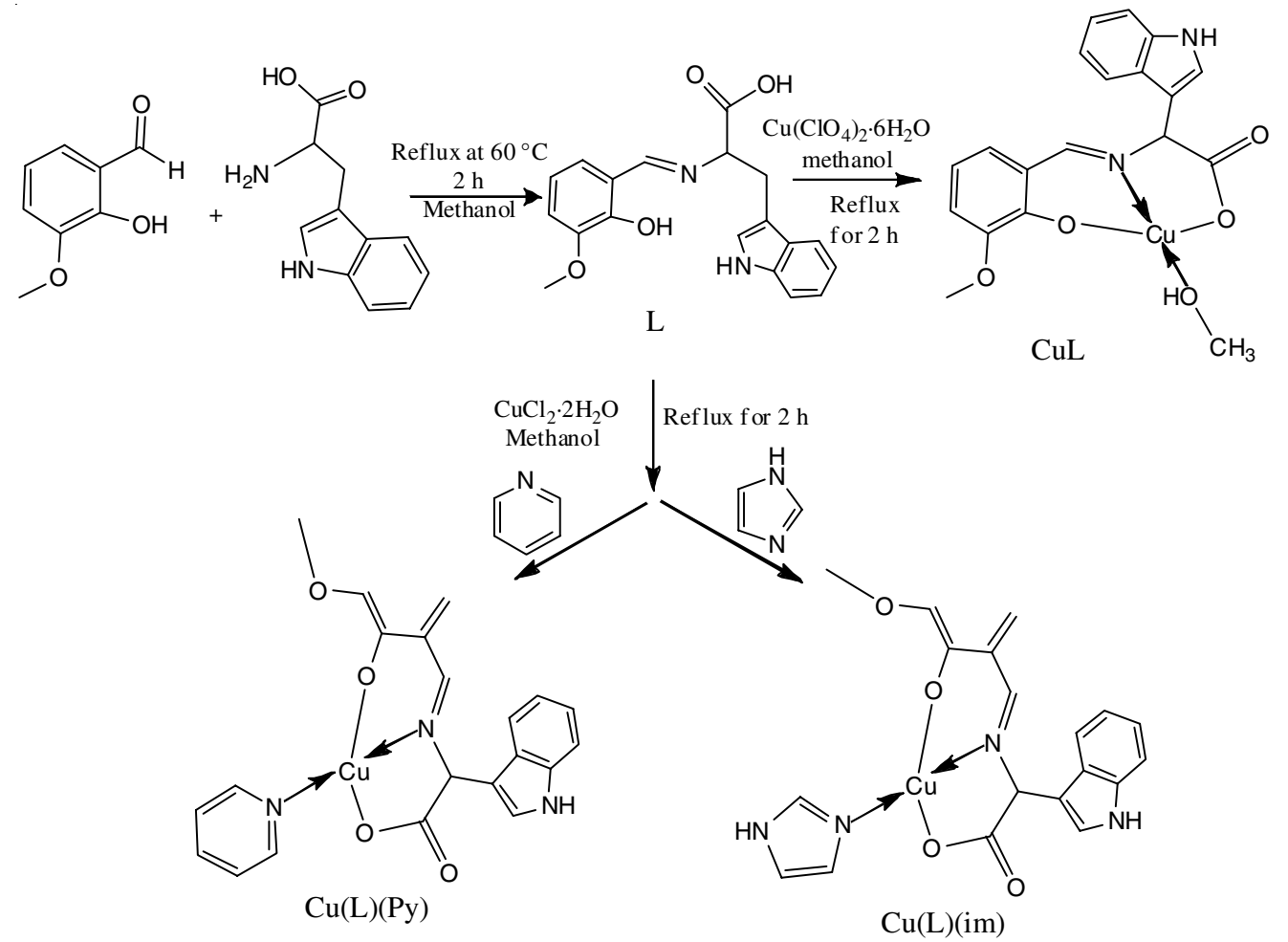
Anticancer activity (cytotoxic effect): The Schiff base ligand (L) and its mixed ligand and binary copper complexes formulated as [Cu(L)(A)] and [Cu(L)] (**Scheme-X**) have been synthesized by Subha *et al.* [80] where, A is heterocyclic nitrogen containing co-ligand such as imidazole or pyridine.



Scheme-VIII: Proposed synthetic scheme of ligand and its metal(II) complexes



Scheme-IX: Proposed synthetic reaction for ligand and its Pd(II) complexes



Scheme-X: Synthetic scheme of Schiff base ligand L and its copper(II) complexes

The complexes supposed to interact with DNA *via* groove binding and follow: L < [Cu(L)] < [Cu(L)(Py)] < [Cu(L)(im)] order. The *in vitro* cytotoxic effect of the complexes have been studied and the results showed potential cytotoxicity against breast cancer cells (MCF-7) of human.

A new Schiff base of amino acid has been prepared and used for complexation with Cu(II) salt to form their mixed ligand complexes [CuL(A)] (Fig. 13) using diimine compounds as co-ligand A that may be 1,10-phenanthroline, 2,2′-bipyridine or 5,6-dimethyl-1,10-phenanthroline [81]. These metal complexes have DNA binding ability and showed the cytotoxic effect against breast cancer cells (MCF-7). All the synthesized compounds also have *in vitro* antioxidant activity in the following order: Schiff base < [Cu(L)bpy] < [Cu(L)dmphen] < [Cu(L)phen].

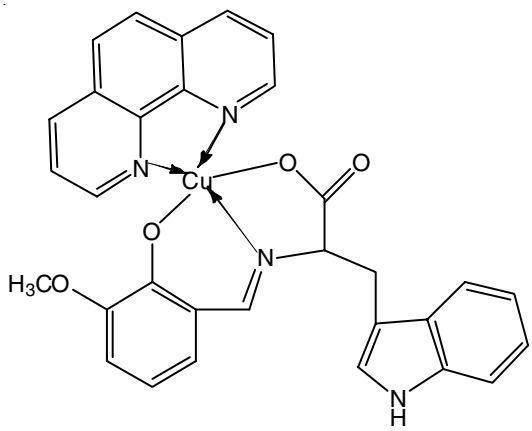


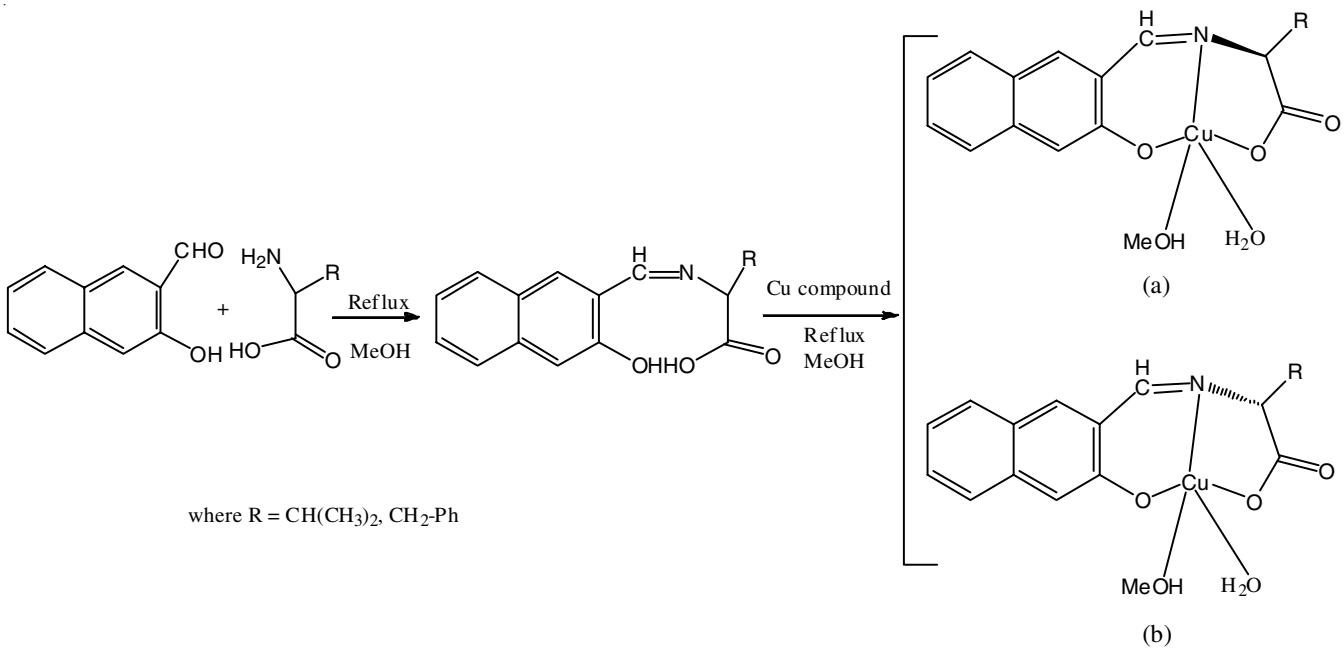
Fig. 13. Proposed structure of [Cu(L)phen] metal complex

Zehra *et al.* [82] synthesized the chiral enantiomeric Cu(II) complexes (**1a**, **1b**, **2a** and **2b**) with amino acid based Schiff bases. The ligands were prepared by reaction of 2-hydroxy-naphthaldehyde with L/D-valine (**1a**, **1b**) or L/D-phenylalanine (**2a**, **2b**) amino acids (**Scheme-XI**). The *in vitro* cytotoxicity of all the enantiomeric complexes have been investigated against some human cancer cells and remarkable cytotoxicity has been explored for L-enantiomeric form of complex **2a** owing to its more lipophilicity. The binding profile with the biomolecular target *ct*-DNA/tRNA revealed that complexes interact with greater binding affinity with L-enantiomers and show greater binding with the tRNA molecule in comparison to *ct*-DNA.

Antidiabetic activity: Lakshmi *et al.* [83] reported the synthesis and characterization of new complexes of copper(II) such as $[CuL_1(tmen)]$ and $[Cu_2(L_2)_2(tmen)]$ derived from tridentate O, N and O donor Schiff bases H_2L_1 and H_2L_2 with tmen (N,N,N′,N′-tetramethylethylene-1,2-diamine). *In vitro* antidiabetic activity of these complexes was high in comparison to standard drug (acarbose). Since copper complexes showed a significant inhibitory effect, so these complexes possibly used as antidiabetic candidate.

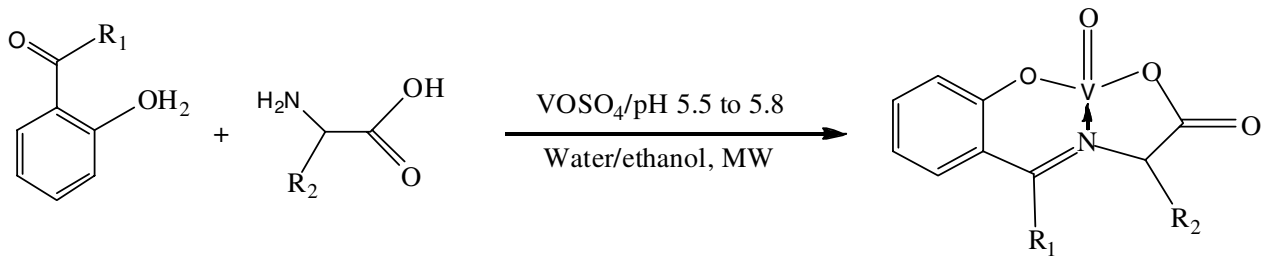
Antioxidant (scavenging activity) and larvicidal activity: Wazalwar & Bhave [84] synthesized some Schiff base complexes of vanadium by a more efficient microwave assisted method (**Scheme-XII**). The antioxidant activity of all the synthesized compounds were measured by DPPH method. Some of these compounds have higher antioxidant activity rather than reference compound ascorbic acid and it was found that the presence of methyl group at α-position to carbonyl group encourage this activity.

Lakshmi & Geetha [85] synthesized number of mononuclear Schiff base complexes [ML(tmen)] (Fig. 14) with selective metal ions and Schiff base ligand synthesized by amino acid and 2′-hydroxyacetophenone. The antioxidant scavenging activity tested by DPPH method and all the synthesized metal complexes showed moderate activity with following order: [CuL(tmen)] > [NiL(tmen)] > [ZnL(tmen)] > [CoL(tmen)]. The larvicidal activity of these compounds was observed against *Culex quinquefasciatus*. The % mortality order is [CuL(tmen)] > [ZnL(tmen)] > [NiL(tmen)] > [CoL(tmen)] > L. They also



where R = $CH(CH_3)_2$, CH_2-Ph

Scheme-XI: Synthetic route for amino acid Schiff base and their copper(II) complexes



Scheme-XII: Synthesis of metal complex

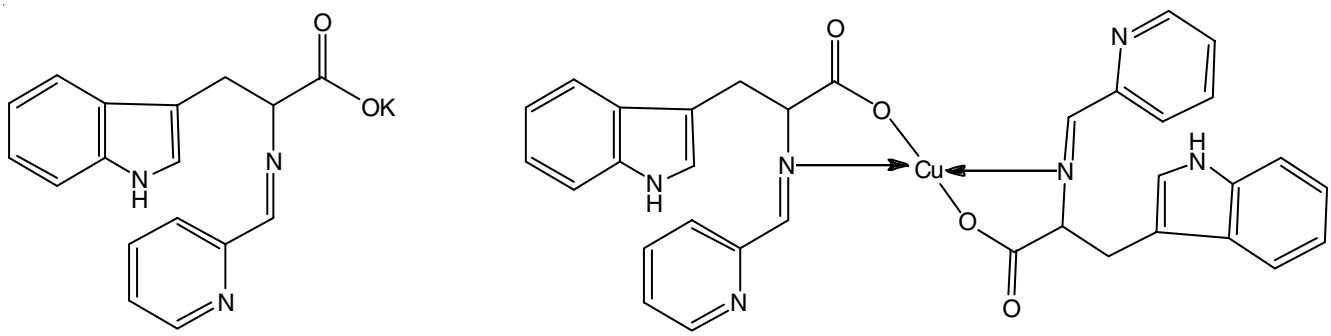


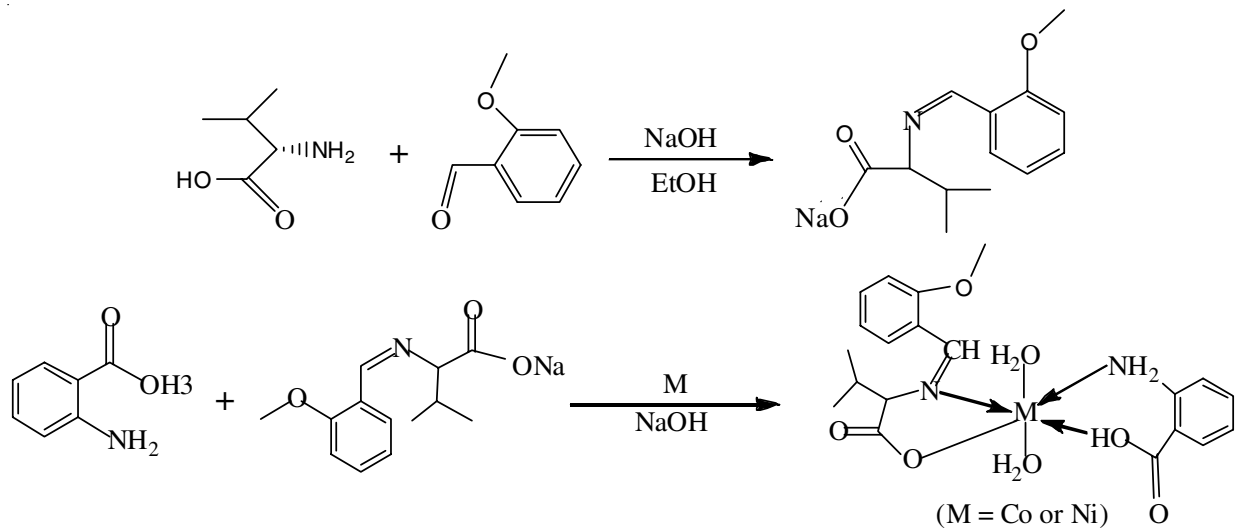
Fig. 14. Structure of ligand (L) and its Cu(II) complex

have good antimicrobial activity against various bacterial and fungal strains.

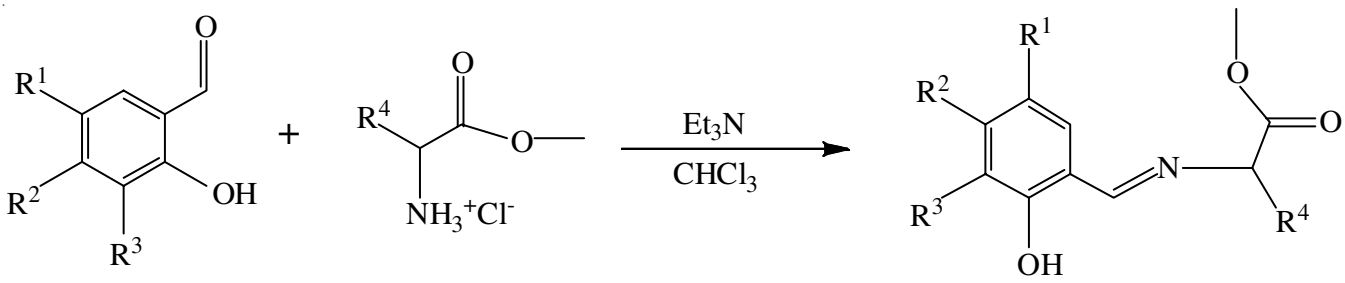
A new Schiff base ligand (L_1) has been synthesized by Kubra *et al.* [86] from 2,6-diaminopyridine and *o*-hydroxy benzaldehyde and further used as ligand for synthesis of metal complex-I and L-cysteine (L_2) used as co-ligand. Further, they have synthesized Schiff base ligand from vanillin and histidine, using it as L_1 ligand in metal complex-II and 2,6-diamino-pyridine (L_2) used as co-ligand. Both types of metal complexes having general formula; $[Cu(II)L_1L_2]$ showed a significant anti-oxidant activity studied by H_2O_2 method and larvicidal activity tested against *C. quinquefasciatus*. In both studies, complex-I have higher activity than complex-II.

Salem *et al.* [87] synthesized a Schiff base (*z*)-2-(2-methoxy-benzylideneamino)-3-methylbutanoic acid derived from valine and 2-methoxybenaldehyde and formed their metal complexes with Co and Ni salt (**Scheme-XIII**). They observed the anti-oxidant activity using DPPH method and antimicrobial activity using the disc diffusion method. The Schiff base and its Ni complex showed greater antioxidant activity rather than Co complex. But Co complex have higher antimicrobial activity in comparison to ligand and its Ni complex, against various Gram-positive and Gram-negative bacteria and some fungi strains.

Antiproliferative activity: Tas *et al.* [88] synthesized some new Schiff base ligands from selective amino acid derivatives condensed with some salicylaldehyde derivatives (**Scheme-XIV**). The antiproliferative activity of all the Schiff bases were observed employing MTT cell proliferation assay. It was found that these compounds are significant pharmacological active supposed due to the presence of Br, OH, OCH_3, Ph, *etc.* bio-active substituents. The highest antiproliferative activity found



Scheme-XIII: Proposed reaction scheme for synthesis of Schiff base and its metal complexes



Scheme-XIV: Proposed reaction scheme for amino acid Schiff base synthesis

for those compounds which have phenyl substituents. All these compounds also acted as an anticancer agents screened by the LDH cytotoxicity kit. Presence of phenyl and bromo-group and their position affect the cytotoxic activity.

Camacho *et al.* [89] reported the synthesis of some new tributyltin(IV) derivatives of Schiff bases and characterized. The compounds are prepared by condensation of some amino acids and 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde. All the novel compounds are exhibited anti-proliferative activity, some of them does not show cytotoxic activity depending on the side chain present in amino acid. Alanine and isoleucine show more cytotoxic effect than the other amino acids but these all may act as potential pharmaceutic candidates that can be examined against cancer.

Conclusion

On the bases of above studies, it is concluded that most of the amino acid Schiff bases and their metal complexes are pharmacological bioactive compounds because these have one or more activity out of antibacterial, antifungal, anticancer, antidiabetic, antioxidant, antiproliferative and larvicidal activities. All the synthesized metal complexes have greater antimicrobial activity in comparison to free Schiff base ligand and the presence of azomethine group containing nitrogen as donor atom play a vital role in encouraging efficiency. Among transition metal complexes, copper complexes having highest antimicrobial and antioxidant activity in most of cases, this study make copper more efficient as bioactive agent. But the lanthanide metal complexes are not as efficient as transition metal complexes. In some cases these have even lower activity than free Schiff base ligands. It is also concluded that the metal complexes have more antibacterial activity specifically good inhibition effect against *S. aureus,* rather than antifungal activity. The metal complexes having good binding affinity with DNA, RNA or other human cells can act as good anticancer agent. The cytotoxic effect depends on the side chain (alkyl group) or the substituents like halogen group, methoxy, hydroxy, phenyl, *etc.* Further various biological activities like antimicrobial, antiviral, anti-inflammatory, *etc.* may be evaluated and explored for new developments in the pharmaceutical and medicinal fields for betterment of humanity.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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