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SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF Ni(II) TERNARY METAL COMPLEXES WITH SCHIFF BASE SAICYLALDEHYDE-AMINO ACIDS AND 1,10-PHENANTHROLINE AS LIGANDS

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ABSTRACT

In the present paper, the synthesis of Ni(II) mixed ligand complexes of the type [Ni(salaa)phen]NO_3 are determined where salaa= Salicylidene amino acids schiff base series of L-Glycine, L-Phenylalanine and L-Tyrosine and phen = 1,10- phenanthroline. The environmentally efficient and modern developed method is used for synthesis of mixed ligand complexes. The ligands and their complexes are characterized by elemental analysis, FT-IR spectroscopy and UV-VIS spectroscopy. The Antimicrobial studies were also performed for the mixed ligand complexes. The investigations of the spectral data for the ligands and complexes suggested the octahedral geometry of the coordination of Ni(II) metal with the ligands. Electronic spectrum of Ni(II) complex displayed the d-d transition bands in the region 730–836, 525–615, and 340–450 nm, presumably due to the three spin-allowed transitions. $3A_{2}g \rightarrow 3T_{2}g$, $3A_{2}g \rightarrow 3T_{1}g$ and $3A_{2}g \rightarrow 3T_{1}g$ transitions. The azomethine linkage (-CH=N-) between salicyladehyde amino acids based Schiff bases is described by the IR spectral peak around 1600 cm^{-1}. This band was shifted towards lower frequencies in the spectra of its metal complexes (1595-1510 cm^{-1}) compared with the above Schiff base indicating the involvement of the azomethine nitrogen in coordination with metal ion. The antimicrobial study shows good inhibition zone against bacteria and fungi in the range of 12-28 mm diameter.

1. INTRODUCTION

Imine or azomethine linkage commonly known as Schiff base is an analogue of a ketone or aldehyde in which the carbonyl group (C=O) has been replaced by an imine or azomethine group. The development of complexes of Schiff bases is the field of research, as these coordination compounds are potentially capable of forming stable complexes with various divalent metal ions. Schiff bases and their metal complexes are increasingly being used as catalysts in various biological systems[1], clinical[2], industrial and analytical areas,[3,4] polymers and dyes[5,6] as well as their studies in enzymatic preparations have been confirmed for these compounds. Several studies showed that the presence of a lone pair of electrons in an sp^2 hybridized orbital of nitrogen atom of the azomethine group is of considerable chemical and biological importance. Because of the preparation and synthetic flexibility, and the special property of -C=N group, Schiff bases are generally excellent chelating agents, especially when a functional group like –OH or –SH is present close to the azomethine group so as to form a five or six membered ring with the metal ion. Due to this diversity they have been widely explored for industrial and analytical applications.[7] Moreover, biological activity of this class of compounds still requires further investigation. Both Schiff bases and their metal complexes are interesting research area for investigating new information about newly synthesized compounds.

Schiff base complexes derived from 4-hydroxy salicylaldehydes have strong anticancer activity e.g., against Ehrlich ascites carcinoma (EAC). The Isoxazole derivatives have a variety of applications in biological, pharmacological and also in agrochemical areas. The Schiff bases derived from 3-amino-5-methyl isoxazole and methoxy salicylaldehyde and naphthaldehyde were reported[8] earlier and it was found that antimicrobial activity of metal complexes show increased activity compared to corresponding Schiff bases.

The review have been reported an outline on the synthesis and use of discovery of the Schiff Bases and recent developments on their “metallo-imines” variants. The applications of Schiff bases in organic synthesis such as hetero Diels-Alder reactions in the organometallic complexes and biological active Schiff intermediates have been studied.[9] Also Schiff base complexes derived from heterocyclic compounds have acquired more attention in the field of bioinorganic chemistry because of their biological active complex compound synthesis. Some heterocyclic-ketone derived Schiff bases show bactericidal property and some others can act as antibacterial agent also.[10-13]

This paper describes the synthesis of Cu(II) ternary mixed ligand metal complexes with the new ligands combinations of salicylaldehyde amino acid series along with 1,10-

phenanthroline and thiourea and their characterization by NMR, FT-IR, UV-VIS and elemental analysis, as well as the antibacterial studies.

2. EXPERIMENTAL

The reagents were obtained commercially from CDH chemicals which were all of AR grade and used as received. The chemicals used during experimental procedure includes amino acids, L-Glycine, L-Phenylalanine and L-Tyrosine, Salicylaldehyde, KOH is used as a base catalyst for the synthesis of Schiff base ligand, 1,10-Phenanthroline. H_2O is used as a heterocyclic secondary ligand. Metal salt $Ni(NO_3)_2$. $_6H_2O$ is used to form mixed ligand complexes. Ethanol is used as a solvent for organic reagents and double distilled water for dissolving polar compounds such as amino acids.

Synthesis of Schiff Base: The synthetic procedures for Schiff base ligands were performed by two ways. They are discussed as under:

Reflux Method: The above mentioned starting materials were used in the synthesis of Schiff base ligand by conventional routes in a reflux condenser at 40°c for 2-3 hours in an ethanol solvent. The equimolar quantity of salicylaldehyde and amino acids (3 mmol.) were allowed to reflux in the presence of KOH (3 mmol.) as a base catalyst. Yellow coloured solution is obtained in the reaction mixture which was kept for 5-7 days for slow evaporation. The precipitate was filtered and washed with ethanol and recrystallized to get the pure crystals. The crystals were dried in a vaccum dessicator over anhydrous $CaCl_2$.

Pestle mortar grinding method: This is the alternative method used for the preparation of Schiff base ligands performed by a mortar and a pestle made of porcelain. The procedure is completely free of solvent. Reagents of equimolar quantity is combined in a mortar and grinded for 10-15 min. with a pestle. The yellow coloured paste is obtained which changes to a solid powder on continous grinding for another 20 minutes. The product was finally washed and recrystallized from ethanol and dried in air and vaccum dessicator over anhydrous calcium chloride.

Three Schiff base ligands have been synthesized with the condensation of salicylaldehyde and amino acids, i.e, salicylidene glycine (salgly), salicylidene phenylalanine (salphyala) and salicylidene tyrosine (saltyr).

All the reactants and catalyst are similar in either procedures instead the reaction time is reduced to few minutes in grinding method and the product yield is increased to 85-95%.

Synthesis of Ni(II) complexes

Ternary Ni(II) complexes of the type [Ni(salaa)(phen)]NO_3, were synthesized where primary ligand is salaa= salicylidene glycine (salgly), salicylidene phenylalanine (salphyala) and salicylidene tyrosine (saltyr) and secondary ligand is phen= 1,10-phenanthroline. The complexes with different ligand combinations were prepared by following ways:

Synthesis of [Ni(salgly)1,10-phenanthroline]NO_3: To a mixture of L-Glycine (3mmol) and KOH (3mmol) in 10 ml distilled water add 10 ml ethanolic solution of salicylaldehyde (3mmol) and reflux the reaction mixture for 3 hours at 40°C. To this mixture, add dropwise 10ml ethanolic solution of 1,10- phenanthroline and 10 ml aqueous solution of $Ni(NO_3)_2.6H_2O$(3mmol). Again reflux the solution for 2-3 hours at 40°C. A green precipitate was obtained which was isolated by filtration, recrystallisation and finally dried in dessicator.

An alternative grinding method is followed for synthesizing the above mixed ligand copper complexes. The amino acid glycine, KOH and salicylaldehyde of equimolar quantity(3mmol) is combined in a mortar and grinded for 10 -15 min. with a pestle. The yellow coloured paste is obtained which changes to a solid powder on continous grinding for another 20 minutes. To this mixture equimolar 1,10 phenanthroline and $Ni(NO_3)_2.6H_2O$(3mmol). was added and grinded well for 15 minutes. A green coloured solid product is obtained which was finally washed and recrystallized from ethanol and dried in air and vaccum dessicator over anhydrous calcium chloride.

Synthesis of [Ni(salphyala)1,10-phenanthroline]NO_3: To a mixture of L-Phenylalanine (3mmol) and KOH (3mmol) in 10 ml distilled water add 10 ml ethanolic solution of salicylaldehyde (3mmol) and reflux the reaction mixture for 3 hours at 40°C. To this mixture, add dropwise 10 ml ethanolic solution of 1,10- phenanthroline and 10 ml aqueous solution of $Ni(NO_3)_2$. $6H_2O$ (3mmol). Again reflux the solution for 2-3 hours at 40°C. A green precipitate was obtained which was isolated by filtration, recrystallisation and finally dried in dessicator.

The amino acid phenylalanine, KOH and salicylaldehyde of equimolar quantity(3mmol) is combined in a mortar and grinded for 15 min. or more with a pestle. The yellow coloured paste is obtained which changes to a solid powder on continous grinding for 20-30 minutes. To this mixture equimolar 1,10 phenanthroline and $Ni(NO_3)_2.6H_2O$ was added and grinded well for 15-20 minutes. A dark green solid product is obtained which was finally washed and recrystallized from ethanol and dried in air and vaccum dessicator over anhydrous calcium chloride.

Synthesis of [Ni(saltyr)1,10-phenanthroline]NO_3: To a mixture of L-Tyrosine (3mmol) and KOH (3mmol) in 10 ml distilled water add 10 ml ethanolic solution of salicylaldehyde (3mmol) and reflux the reaction mixture for 3 hours at 40°C. To this mixture, add dropwise 10 ml ethanolic solution of 1,10- phenanthroline and 10 ml aqueous solution of $CuNO_3.3H_2O$(3mmol). Again reflux the solution for 2-3 hours at 40°C. A green precipitate was obtained which was isolated by filtration, recrystallisation and finally dried in dessicator.

The amino acid tyrosine, KOH and salicylaldehyde of equimolar quantity(3mmol) is combined in a mortar and grinded for 10 min. or more with a pestle. The yellow coloured paste is obtained which changes to a solid powder on continous grinding for 20minutes. To this mixture equimolar 1,10 phenanthroline and $Ni(NO_3)_2.6H_2O$ was added and grinded well for 15 minutes. A green coloured solid product is obtained which was finally washed and recrystallized from ethanol and dried in air and vaccum dessicator over anhydrous calcium chloride.

3. RESULTS AND DISCUSSIONS

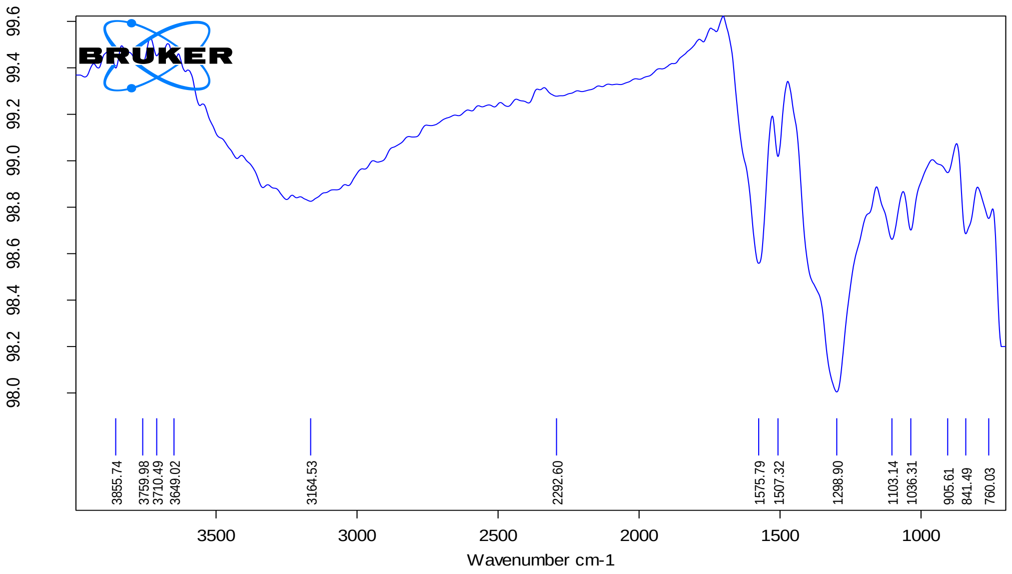
The synthesized complexes have been characterized by spectrophotometric techniques such as UV-Vis spectroscopy and IR spectroscopy. The main results achieved in the course of the present investigation by either methodologies have been discussed here.

IR studies

IR spectra of the ligands and complexes were recorded using KBr pellets in the range (4000–400 cm^{-1}) on Bruker Infrared model. IR spectral studies of ligands explains the formation of azomethine linkage (-C=N) which is observed at 1600-1575 cm^{-1} for different salicylaldehyde based ligands. This region of vibrational stretching are characterstic to the synthesis of Schiff bases. A broad band in the region 3320-3194cm^{-1} is due to N-H streching which coincides with the presence of OH in the amino acid. The carboxylic C=O vibrational modes, symmetric and asymmetric were found at 1575-1507 cm^{-1}. The C-O stretching is observed at 1313 cm^{-1}.

In the comparison of the spectrum of complex and ligand, we observed that the complexes exhibits absorption band of imine group at a lower frequency range by about 14- 20 cm^{-1} from the ligand peaks.[14] This shift of band at lower wave number indicates that the azomethine nitrogen is coordinated to the metal through its lone pair of electrons. The absorption band of phenolic –OH group is lost in the spectrum of complex, it indicates that phenolic –OH group is deprotonated and metal binds through phenolic oxygen. Also the phenolic C-O vibrations is increased to 1312 cm^{-1} in metal complex spectra to suggest the coordination of ligand to the central metal ion. While the bands due to asymmetric and symmetric COO^{-} streching in the region 1594 cm^{-1} and 1495 cm^{-1} represents the coordination of carboxylic group to the metal ion complex formation.

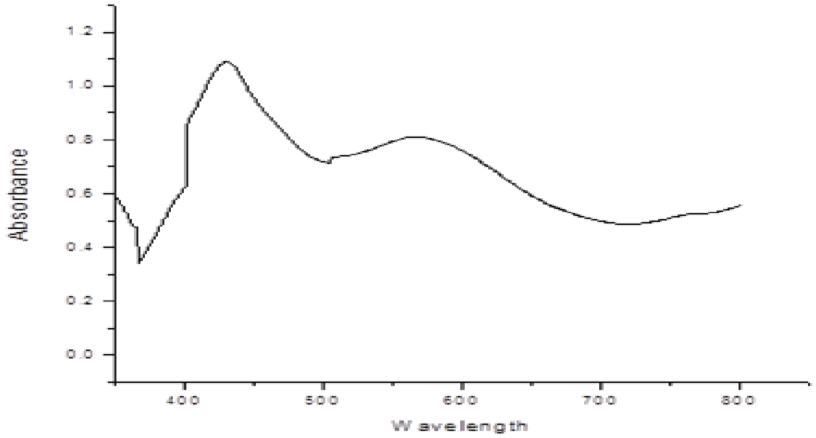
The heterocyclic ligand 1,10-phenanthroline ring stretching peaks were found at higher frequency range 1510 cm^{-1} due to co-ordination of nitrogen atoms to the metal. All the shifts were reported in the complexes synthesized by conventional reflux techniques are in good agreement with the solvent free synthesis.



IR Spectrum of [Ni(salgly)1,10- phenanthroline] complex.

UV Studies

Electronic spectra of metal complexes in DMF were recorded on UV-VIS spectrophotometer. Absorption studies of the Ni(II) complexes were assigned to the ligand field and charge transfer transitions. The electronic spectra of present Ni(II) complexes show three bands at 730–836, 525–615, and 340–450 nm, presumably due to the three spin-allowed transitions. $3A_{2}g \rightarrow 3T_{2}g$, $3A_{2}g \rightarrow 3T_{1}g$ and $3A_{2}g \rightarrow 3T_{1}g$ transitions for octahedral structure.[15,16]



Electronic spectrum of [Ni(salgly)1,10- phenanthroline] complex.

The complexes were soluble in methanol, DMF, DMSO and sparingly soluble in water. They are very stable in solid and dry atmosphere while hygroscopic at lower temperature. Therefore they were stored in a dessicator over anh.$CaCl_2$.

The main results achieved in the course of the present investigation by both the methods have been discussed and compared with each other on the basis of analytical data obtained.

Table 1 shows physiochemical data of Ligands and Complexes synthesized by either methodologies. All the reactants and catalyst were similar in the two procedures instead the reaction time is reduced from hours to few minutes and the product yield is increased to a considerable amount.

Table 1: Physical data of Ligands and Ni(II) Complexes synthesized by two methods

S.No.	Compound Ligand/Ni(II) Complex	M.P (°C)	Colour	Mol.Wt (calcu.)	%Yield(Reflux 4-5hrs)	%Yield(Grinding 30-45min.)
1	SalGlycine	186	Yellow	179.2	63	86
2	Salphenylalanine	194	Pale yellow	287.31	58	90
3	SalTyrosine	215	Pale yellow	303.31	64	84
4	[Ni (salgly)phen]NO_3	324	Dark green	512.5	65	85
5	[Ni(salphyala)phen]NO_3	336	Green	528.4	74	88
6	[Ni(saltyr)phen]NO_3	340	Dark green	541.2	77	90

Antimicrobial studies

The Schiff bases and their mixed complexes were screened for antimicrobial activity against pathogenic bacteria and fungi strains viz. *S. aureus, S. pyogenes, E. coli, P. aeruginosa, C. albicans, A. niger, A. clavatus* using broth dilution method. Petri dish of Muller-Hinton agar (bacteria) and Czapek Dox agar (fungi) were developed and nutrient broth cultures (with swabs) of known bacteria and fungi were grown on the plates. The investigated ligand and its metal complexes are found to be good antimicrobial agents.

The agar medium was seeded with the organisms by pour plate method. Wells of 6mm diameter were created and then filled with the solution. The complex solution were poured into the well using sterile syringe. The plates were incubated at 37ºC+2ºC for one day for bacterial and 25+2ºC for 2-4 days for fungal activity. The plates were pre-incubated for 1 hr at room temperature to ensure adequate diffusion and finally incubated at 37°C for required period. The plates were observed for the zone clearance around the wells.[17,18] The zone of inhibition was calculated by measuring the diameter of the inhibition zone around the well (in mm) including the well diameter.

The ligands as well as synthesized complexes show an remarkable increase in the antibacterial and antifungal activity against most of the species of bacteria and fungi as compared to their free states. The cell damage is observed in the range of 12 mm - 28 mm diameter zone of inhibition.

Table 2: Shows the antibacterial activity against *Staphylococcus aureus* of pure ligand and mixed ligand complex formation.

Ligand/Complex Sample description	Zone of inhibition (in mm)
1,10- phenanthroline	14 mm
Ni(salphyala)1,10-phenanthroline	28 mm
Ni(saltyr)1,10-phenanthroline	23 mm

Fig. a: Antibacterial activity of Ni(salphyala)1,10-phenanthroline complex.

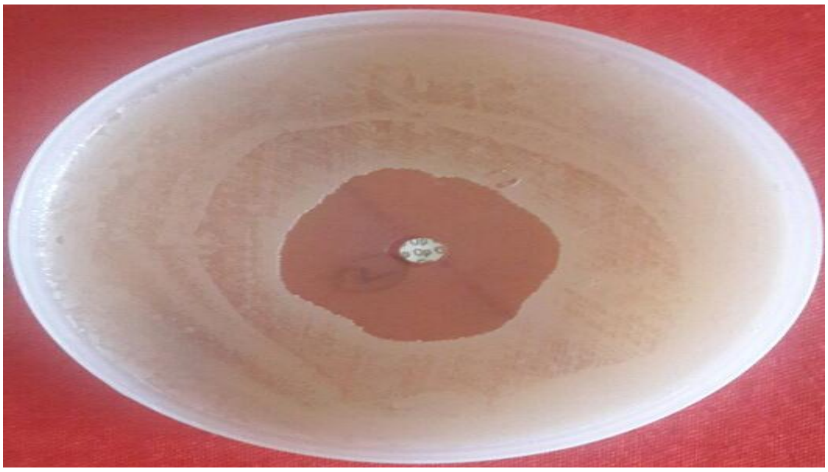


Fig. b: Antibacterial activity of Ni(saltyr)1,10-phenanthroline complex.

Table 3: Shows the antifungal activity against *Candida albicans* of pure ligand and mixed ligand complex formation.

Ligand/Complex Sample description	**Zone of inhibition (in mm)**
1,10- phenanthroline	14 mm
Ni(salphyala)1,10-phenanthroline	21 mm
Ni(saltyr)1,10-phenanthroline	27 mm

The antimicrobial activity can be explained through the figures **a, b and c** which gives the inhibition zone of bacteria and fungi under studies. Metal complexes of nickel(II) shows enhanced activity against *Staphylococcus aureus*, *Candida albicans*, *etc*. The results suggest that synthesized complexes are more effective than the ligands against most of the bacterial and fungal colony.

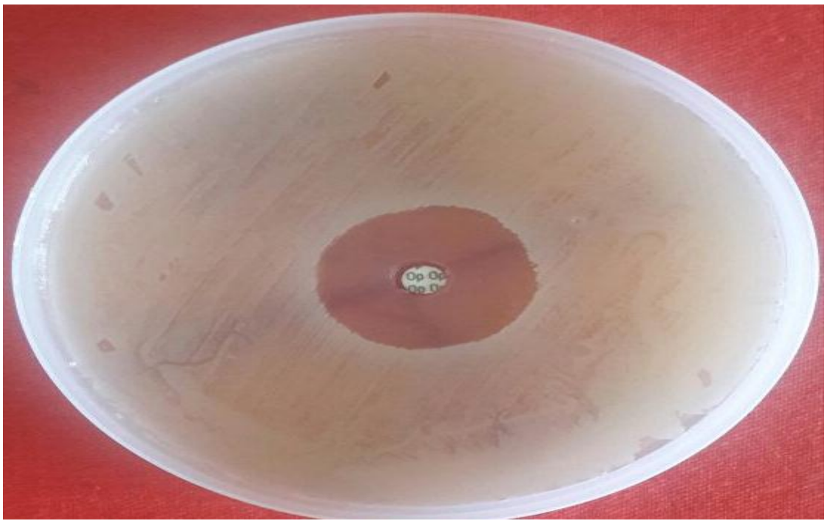


Fig. c: Antifungal activity of Ni(salphyala)1,10-phenanthroline complex.

4. CONCLUSION

The present research included three Schiff base ligands which have been synthesized with the condensation of salicylaldehyde and amino acids, i.e, salicylidene glycine (salgly), salicylidene phenylalanine (salphyala) and salicylidene tyrosine (saltyr). The condensation was preceded through two ways reflux mehod and solvent free pestle mortar grinding method. Also, three Ni(II) mixed ligand green coloured complexes have been synthesized as [Ni(salgly)phen]NO_3, [Ni(salphyala)phen]NO_3, [Ni(saltyr)phen]NO_3 complexes, using reflux and grinding procedures.

The pestle mortar assisted method is very rapid, simple and economic for the preparation of both ligands and Ni(II) complexes. The reflux method involves excessive application of laboratory equipments, conditions, solvent and time consuming reaction steps with average product yields. Contrary to this, the pestle mortar assisted synthesis is very fast and requires lesser laboratory conditions such as glasswares, instruments etc. It is completely free of solvent which is a contribution in the scope of the green synthesis chemistry.

The comparison of the synthesis of ligand and complexes performed through physiochemical and spectroscopic techniques, i.e, IR, UV-Vis spectral data obtained from either method, conventional and solventless procedure are in good agreement with one another. The azomethine linkage(-CH=N-) between salicylaldehyde amino acids based Schiff bases is described in the spectral studies and the shifts were observed due to the complexation of ligands with metal ions.

The Antimicrobial studies were also performed for the synthesized Ni(II) mixed ligand metal complexes and pure ligands. The antibacterial and antifungal screening is found to be enhanced for the complexes under investigation. Therefore the ease of Salicylaldehyde amino acid based Schiff bases and heterocyclic diimine ligands mixed together in co-ordination makes an attractive approach to study of the novel path for coordination metal complexes.

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