SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF SCHIFF BASE METAL COMPLEX

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ABSTRACT:

A drug is a chemical substance used in the treatment, cure, prevention, or diagnosis of disease. Many drugs are used to treat infectious diseases caused by microbes. Today antibiotics are most commonly used in treating various infectious diseases. The development of more potent metal based drugs has been under investigations over the lost three decade, and it has been discover that inorganic compounds have enormous impact in medicine. One such complex is Schiff base metal complex, which are condensation products of primary amines and aldehydes or ketones (RCH=NR’). These complexes containing certain metal ions are active in many biological processes.

The present study concludes with the synthesis, characterization, and biological activity of Schiff base Cd (II) complex, prepared from thiosemicarbazide and acetylacetone. The Schiff base and its metal complex are characterized by IR, NMR, and MASS Spectroscopy. Their antibacterial and antifungal activities have also been done.
INTRODUCTION

Schiff bases and their chemistry

Nowadays, coordination compounds are important for the betterment of human welfare. The example of such type of complex is Transition metal complex derived from Schiff base.

The compounds containing azomethine (-CH=N-) group are known as Schiff bases, are formed by condensation of primary amines with a carbonyl compounds such as aldehydes or ketones.

\[
\text{R-NH}_2 + \overset{\text{O=C-R}}{\text{H}} \rightarrow \text{R-N=CH-R} + \text{H}_2\text{O}
\]

Primary amine Aldehyde Schiff base

Where R may be an aliphatic or an aromatic group.

Schiff bases are characterized by –N=CH- (imine) group which is important in elucidating the mechanism of transamination and racemisation reactions in biological systems. Schiff bases of aliphatic aldehydes are relatively unstable and are readily polymerizable while those of aromatic aldehydes, having an effective conjugation system, are more stable. The condensation of amines with aldehydes and ketones have numerous applications which include preparative use, identification, detection, and determination of aldehydes and ketones, purification of carbonyl or amino compounds, or protection of these groups during complex or sensitive reactions. Schiff bases are generally bi- or tri-dentate ligands capable of forming very stable complexes with transition metals.

Among the organic reagents actually used, Schiff bases possess excellent characteristics, structural similarities with natural biological substances, relatively simple preparation procedures and the synthetic flexibility that enables design of suitable structural properties.
LITERATURE SURVEY

1. T.G. Miller reported that the Schiff base prepared from 4-(di-chloromethyl)-4-methyl-2,5-cyclohexadien-1-one and the alkyl amines, cyclohexylamine and butyl amine, they react at elevated temperature with the corresponding primary amine to give N-alkyl-p-toluidines and N, N’-dialkylformamides. If trace of water are present, the N,N’-dialkylformamides are partly hydrolyzed to N-alkylformamides. When the Schiff bases are heated alone, they undergo a highly exothermic reaction complete carbonization.

2. Dow Chemical Co. analyzed esters of Schiff base carbamates, and its pesticides and parasiticides activities. They analyzed that the reactions of aromatic aldehydes with aminophenols and of hydroxylaldehydes with anilines formed Schiff bases which reacted with MeNCO and yielded carbamate esters. It was observed that these carbamates are effective against aphids and acarides.

3. Moszew et al. proposed new compounds from aroylthioacetic and aroylmalonic acids. This simple Schiff base were obtained by reacting acetophenone, and p-methyl and p-chloroacetophenone with some aromatic amines such as aniline, 3-aminopyridine by treating these bases with esters R²NCSof isothiocyanic acid R²N:CR¹CH₂CSNH₃(II) are obtained.

4. Michel Contc. et al. have synthesized and analyzed the physiochemical properties of Schiff base in benzothioles series. The prepared compound 2-aminobenzothiazole, m. 129°C, 2-imino-3-methylbenzothiazoline, m. 122°C, 2-formylbenzothiazole, m. 70°C are prepared according to known method. NMR and UV data are given.

5. Datta et al. analyzed the synthesis of azetidinones bearing a 2-chloroquinoline-3-carboxyaldehyde moiety in 60-75% yields by condensation reaction of chloroacetyl chloride and the corresponding N-aryl(2-chloroquinolin-3-yl) azomethines and their antimicrobial activities were studied.

6. Bagihalli et al. were reported Cobalt(II), nickel(II) and copper(II) complexes of Schiff bases derived from 3-substituted-4-amino-5-mercapto-1,2,4-triazole and 8-formyl-7-hydroxy-4-methylcoumarin show potent antibacterial activity against Escherichia coli, Staphylococcus aureus, and antifungal activities against Aspergillus niger. Chitrapriya et al. were reported the Ru(II)–PPh3/AsPh3 complexes, containing hydrazine oxime ligands, show considerable
activity against selected bacterial species and are capable of binding to Herring sperm DNA in mixed modes.

7. Tossadis et al were reported The remarkable biological activity of acid hydrazides R-CO-NH-NH2, a class of Schiff base, their corresponding aroylhydrazones, R-CO-NH-N=CH-R’ and the dependence of their mode of chelation with transition metal ions present in the living system have been of significant interest in the past. Barwa et al Schiff bases have often been used as chelating ligands in the field of coordination chemistry and their metal complexes are of great interest for many years. It is well known that N and S atoms play a key role in the coordination of Hugo Schiff was first reported Schiff base in 1864. Schiff bases can be prepared by condensing carbonyl compounds and amines in different conditions and in different solvents with the elimination of water molecules. The presence of a dehydrating agent normally favours the formation of Schiff bases.

8. Barwa et al Schiff bases have often been used as chelating ligands in the field of coordination chemistry and their metal complexes are of great interest for many years. It is well known that N and S atoms play a key role in the coordination of compound.

9. Hugo Schiff was first reported Schiff base in 1864. Schiff bases can be prepared by condensing carbonyl compounds and amines in different conditions and in different solvents with the elimination of water molecules. The presence of a dehydrating agent normally favours the formation of Schiff bases.

10. Jursik et al were proposed reactions of ligands containing coordinated azomethine group. And copper(II) complexes derived from α-aminodicarboxylic acids and salicyldehyde. They reported that the effect of reduction of electron at α-C atom on the electrophilic substitution at this atom in Cu(II) complexes derived from α-aminodicarboxylic acids and salicyldeyh

**EXPERIMENTAL**

All Reagents and Chemicals were of analytical grade and used without further purification. All Chemicals and solvent such as thiosemicarbazide, Acetylacetone, cadmium acetate dehydrate, methanol and ethanol were purchased from Sd Fine Chemical Limited Mumbai.
SYNTHESIS OF SCHIFF BASE:

2,4 Pentanedione (acetylacetone) (5mmol, 0.5ml) was added dropwise to Solution of thiosemicarbazide (10mmol, 0.910gm) in methanol (15ml) with continuous stirring at 70°C for 20 hours with refluxing a yellow colour solution was removed by filtration and recrystallized from (1:1) (V/V) MeOH/EtOH Solution the crystalline Product was dried in a dessicator.

SYNTHESIS OF SCHIFF BASE Cd(II) COMPLEX:

The crystals of the ligand (2.7mmol, 0.670gm) and cadmium acetate dihydrate (2.7mmol, 0.718gm) were dissolve in ethanol (60ml) and mixture was refluxed at 65°C for 6 hours. A yellow colour precipitate was obtained and washed with ethanol and dried in a dessicator.

CHARACTERIZATION

The Schiff base Ligand and its Cd (II) complex are characterized by IR, ¹HNMR, and MASS Spectroscopy.

INFRARED SPECTRA:

The selected infrared spectrum of schiff base and its metal complex are reported in table I.
The infrared spectrum of the schiff base shows characteristic bands due to $\nu (N-H)$, and $\nu(C-H)$ around $3377.71 \text{ cm}^{-1}$ and $2996.98 \text{ cm}^{-1}$, respectively. Another bands $1596.82 \text{ cm}^{-1}$, $1106.73 \text{ cm}^{-1}$, $1026.03 \text{ cm}^{-1}$ and $635.15 \text{ cm}^{-1}$ are assigned to $\nu(C=N)$, $\nu(C=S)$, $\nu(C-N)$ and $\nu(C-S)$ respectively. The infrared spectrum of metal complex shows characteristic bands due to $\nu(N-H)$, $\nu(C=N)$ and $\nu(C=S)$ around $3379.81 \text{ cm}^{-1}$, $1548.42 \text{ cm}^{-1}$ and $1021.85 \text{ cm}^{-1}$ respectively. Another band $678.64 \text{ cm}^{-1}$ and $618.10 \text{ cm}^{-1}$ arise due to $\nu (M-N)$ and $\nu (M-S)$ bonds show metal is coordinate with N and S at atoms of Schiff base.

In comparison with the spectrum of schiff base, metal complex bands exhibit a downward shift (40-80 $\text{ cm}^{-1}$) of $\nu(C=N)$ and $\nu(C=S)$ indicating the participation of azomethine nitrogen and sulfur atoms in coordination to metal ion.

$^1$$H$ NMR SPECTRA:

The $1H$ NMR Spectrum of Schiff base exhibit signals (singlet) at $\delta1.2610$, $\delta2.3684$, $\delta3.7764$ and $\delta5.9070 \text{ ppm}$ which arise due to -CH$_3$, -CH$_2$, -NH$_2$ and -NH- protons respectively.

In the case of Cd (II) complex, the signal (singlet) of -CH$_3$, -CH$_2$, -NH$_2$ and -NH- protons were found at $\delta1.2478$, $\delta2.3449$, $\delta3.7277$ and $\delta5.8417\text{ppm}$ respectively in the spectrum. The lower values chemical shift in case of metal complex shows the shielding of
protons that indicated the participation of azomethine nitrogen and sulfur atoms of ligands in coordination with metal ion.

The selected $^1$H NMR spectrum of schiff base and its metal complex are reported in table 2.

Table: 2

<table>
<thead>
<tr>
<th>Protons</th>
<th>-CH$_3$</th>
<th>-CH$_2$</th>
<th>-NH$_2$</th>
<th>-NH-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ligand</td>
<td>(s)$\delta$ 1.2610</td>
<td>(s)$\delta$ 2.3684</td>
<td>(s)$\delta$ 3.7764</td>
<td>(s)$\delta$ 5.9070</td>
</tr>
<tr>
<td>Complex</td>
<td>(s)$\delta$ 1.2478</td>
<td>(s)$\delta$ 2.3449</td>
<td>(s)$\delta$ 3.7277</td>
<td>(s)$\delta$ 5.8417</td>
</tr>
</tbody>
</table>

MASS SPECTRA:

The mass spectrum of schiff base shows a molecular ion peak at m/z= 285.092 which is equivalent to its molecular weight [(L+3H$^+$).2H$_2$O].

The fragment ion peaks in the mass spectrum leads to formation of the species $[C_4N_4SH_7]^+$ and $[C_3N_3SH_{10}]^+$ arise at m/z= 155 and m/z= 132. The other ion peaks such as $[L+4H^+].2H_2O$ and $[L+5H^+].2H_2O$ are appear at m/z= 286 and m/z= 287 in the mass spectrum.

In mass spectrum of Cd (II) complex shows a molecular ion peak $[M]^+$ at m/z= 358 that is equivalent it its molecular weight. The fragment ion peaks in the mass spectra lead to formation of the species $[M-2H^+]$ which arise at m/z= 356. And other ion peaks arise at m/z= 376, m/z= 373 and m/z= 372 due to formation of species $[M+H_2O]$, $[M-3H^+].H_2O$ and $[M-4H^+].H_2O$.

Antibacterial Activity -

The bacteria were taken from the Institute of Bioscience and Biotechnology I.B.S.B.T. C.S.J.M. University Kanpur. The antibacterial activity of the Schiff base Cd(II) complex was performed by following process.

Test microorganism and growth of plant-

The test microorganism, used for the antibacterial activity screening was Escheichia Coli, Psedomonas, Salmonella and Staphylo.
Preparation of Broth Media-

Peptone - 0.5g
NaCl - 0.5g
Breif Powder Extract - 0.5g

Preparation of Nutrient Agar Media-

Peptone - 1.00g
NaCl - 1.00g
Breif Powder Extract - 0.60g
Agar - 4.0g

Preparation of Inoculum-

Bacteria were cultured over night at 28°C for twenty four hours in Muller Highton broth are used as Inoculum.

Preparation of plates-

Sterile Petri dish with a diameter of six centimeter plates were prepared by pipetting 100 μ l volume of stock solution of metal complex on to sterile blanks plates. The plates were air tied and then stocke solution at 4°C used within two days, a plate containing metal complex solution was applied to inoculated plates by using framed forceps.

Procedure-

Bacteria stain (Escheichia Coli, Psedomonas, Salmonella and Staphylo) were inoculated in five milliliter nutrient broth media (NB) and incubulated at 28°C for twenty hours. Nutrient Agar (NA) plates were prepared and spreaded with 100 μ l bacterial culture and seven millimeter wells were cut in PDA plates. Wells were filled with purified compound solution of methanol at concentration of 100 mol/ml. Then plates are incubulated at 28±2°C for twenty four hours.
Analysis and measurement-

These organism were indentified and procured from Microbiology Department of C.S.J.M. university Kanpur.

Results-

The result obtained is prepared in table. The antibacterial activity of Schiff base Cd(II) complex.

Table3. Antibacterial activity of Schiff base metal complex.

<table>
<thead>
<tr>
<th>Compound (concentration)</th>
<th>Antibacterial activity zone of inhibition (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E.coli</td>
</tr>
<tr>
<td>Schiff base Cd(II) complex (50μl)</td>
<td>1.3</td>
</tr>
<tr>
<td>Schiff base Cd(II)complex(50μl)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

From above Table3. it is appear that shiff base Cd(II) complex show antibacterial against E.coli, Pseudomonas, Salmonella and Staphylo bacteria

Antifungal activity-

Test microorganism and growth culture-

The seleretorium and Macrophomina phasealina was taken from Department of Microbiology I.B.S.B.T. C.S.J.M. university Kanpur.

Fungi and their maintenance-

The fungi were isolated from the infected part of their respective hosts via Alternaria brassicea sub culture from laboratory stain. Fungi were cultured on potato dextrose agar (PDA) medium at 25±2°C and were purified by signal spore germination on PDA slant and store at 4°C for further use.
Composition of PDA medium:

- Peeled Potato: 250g
- Dextrose: 20g
- Agar: 20g
- Distilled water: 100ml

Detection of antifungal activity:

The purified compound in respective solvent was tested for their antifungal activity by silica gel thin layer chromatography (TLC) method. Different solution of metal complex were prepared 20 μl of each concentration was spotted on TLC plates, dried at room temperature and overspread with spore suspension (1×10^7 spore/ml) of test fungi in PDA medium.

The plates were incubated in humid chamber at 25±2°C for three or four days until the growth of the fungus become visible and a control plates, spotted with the corresponding organic solvent was run in parallel. The minimum inhibitory concentration (MIC) was defined as the minimum concentration at which on fungal growth was observed that is showing a clear zone of inhibition.

Result:

Table 4. Antifungal activity of Schiff base Cd(II) complex

<table>
<thead>
<tr>
<th>Compound</th>
<th>Antifungal activity zone of inhibition (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seleretorium</td>
<td>Macrophomina phasealina</td>
</tr>
<tr>
<td>Schiff baseCd(II) complex</td>
<td>0.8</td>
</tr>
</tbody>
</table>
REFERENCES

Fig. 1: 1HNMR spectrum of ligand

Fig. 2: IR spectrum of ligand
HNM R SPECTRUM OF LIGAND
Fig. 6: Mass spectrum of metal complex
CONCLUSION

The present study concludes with the synthesis, characterization and antimicrobial activity of Schiff base Cd (II) complex derived from thiosemicarbazide and acetylacetone was refluxed in (2:1) molar ratio and this Schiff base was formed metal complex by reaction with Cadmium acetate dihydrate. The compound were characterized by IR, $^1$H NMR, and MASS spectroscopy. In the IR spectra of Schiff base and its metal complex the C-H, N-H, C=N, C=S, M-N, and M-S bands were identified. The $^1$H NMR study supported the structure regarding the presence of -CH$_3$, -CH$_2$, -NH-, and -NH$_2$, protons in the Schiff base and metal complex. The molecular weight of Schiff base and metal complex were calculated with help of mass spectra.

The antimicrobial study showed that the metal complex was biologically active against both bacteria and fungi.
2,4 Pentanedione (1 mol) + Thiosemicarbazide (2 mol) → -2H₂O → Schiff base → Cd(CH₃COO)₂·2H₂O → Schiff base Cd(II) complex

Synthesis of Schiff base metal complex