EVALUATION OF ANTIMICROBIAL ACTIVITY OF CU(II), NI(II), CO(II) AND MN(II) METAL CHELATES OF SCHIFF BASES

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ABSTRACT

The complexes of schiff base possess remarkable antibacterial property. Review of literature also indicate that the metal complexes are better antimicrobial agents as compared to free schiff bases. In the present work we discuss about the antibacterial activity of Cu(II), Ni(II), Co(II) and Mn(II) metal chelates of 4-methyl[(5ʹ-naphthylazo-2ʹ-hydroxybenzylidene) amino] benzene and Cu(II), Ni(II), Co(II) and Mn(II) metal chelates of N,Nʹ-bis(2-hydroxybenzylidene)-1,2-diaminobenzene. The complexes have been screened for their in vitro antibacterial activity against three bacteria, Lactobacillus, S.aureus and K.aerogenes. The Copper complexes were shown to possess more antibacterial activity than the other Schiff-base complexes.

Key words: K.aerogenes., benzene, metal chelate.

INTRODUCTION

Compounds containing an azomethine group (-CH=N-), known as Schiff bases are formed by the condensation of a primary amine with a carbonyl compound. 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. Schiff bases have number of applications viz., preparative use, identification, detection and determination of aldehydes or ketones, purification of carbonyl or amino compounds, or protection of these groups during complex or sensitive reactions. They also form basic units in certain dyes.

Schiff bases are generally bi-or tri-dentate ligands capable of forming very stable complexes with transition metals. Some are used as liquid crystals. In organic synthesis, Schiff base reactions are useful in making carbon-nitrogen bonds.
Schiff bases appear to be an important intermediate in a number of enzymatic reactions involving interaction of an enzyme with an amino or a carbonyl group of the substrate. One of the most important types of catalytic mechanism is the biochemical process which involves the condensation of a primary amine in an enzyme usually that of a lysine residue, with a carbonyl group of the substrate to form an imine, or Schiff base.

Schiff bases derived from an amino and carbonyl compound are an important class of ligands that coordinate to metal ions via azomethine nitrogen and have been studied extensively (Vigato et al., 2004). In azomethine derivatives, the C=N linkage is essential for biological activity, several azomethine has been reported to possess remarkable antibacterial, antifungal, anticancer and antimalarial activities (Bahl and Bahl, 1996; Barboiu et al., 1996). The complexes of Copper, Nickel, Cobalt and Manganese with Schiff bases have wide applications in food industry, dye industry, analytical chemistry, catalysis, fungicidal, agrochemical, anti-inflammable activity, antiradical activities and biological activities (Gemiet et al., 2004; DhivyPriya et al., 2013; RishuKatwalet al., 2012; Amiri, 2012; Avijganet et al., 2006; Chalchat et al., 2008).

Schiff bases, products of the reaction of primary amines and carbonyl compounds, are involved in many metabolic processes. Numerous products of further fragmentation and crosslinking are responsible for the color, flavor, and taste of foods and drinks (Matijevic-Sosa et al., 2006).

In the present work were report the antibacterial activity of Cu(II), Ni(II), Co(II) and Mn(II) metal chelates of 4-methyl[(5′-naphthylazo-2′-hydroxybenzylidene) amino] benzene and Cu(II), Ni(II), Co(II) and Mn(II) metal chelates of N,N′-bis(2-hydroxybenzylidene)-1,2-diaminobenzene.

**Key Word:** Antimicrobial activity, Cu(II), Ni(II), Co(II) and Mn(II)

**MATERIALS AND METHODS**
**Synthesis of metal chelates of 4-methyl [(5′- naphthylazo-2′- hydroxybenzylidene) amino] benzene**

Ice cold solution of aniline(0.3mol) in few drops of 1:1 HCl is mixed with ice cold saturated solution of sodium nitrite in water. The solution is stirred well. To this ice cold solution of salicylaldehyde(0.3mol) in sodium hydroxide is slowly added with stirring. A red orange
precipitate obtained is filtered, washed with water and dried. Hot ethanolic solution of the above precipitate (0.2mol) is refluxed with p-toludine (0.2mol) in alcohol for about 15 minutes, stirred and poured into crushed ice, filtered washed and dried. Recrystallised from alcohol. Red coloured crystals of 4-methyl[(5ʹ-naphthylazo-2ʹ-hydroxybenzylidene) amino] benzene (MNAB) is formed.

MNAB (0.02mol) is mixed with the alcoholic solution of metal chloride (0.01mol). The mixture was refluxed for about 2 hours. The mixture was shaken well and cooled. The solid obtained was filtered and dried. The crystals were recrystallised with a mixture of methanol, ethyl acetate and ether and finally dried under reduced pressure over anhydrous CaCl₂ in a desiccator. The progress of the reaction and purity of the product was monitored by TLC using silica gel G. The structure of the compound was established by using physical, analytical and spectral data.

**Synthesis of metal chelates of N,Nʹ-bis(2-hydroxybenzylidene)-1,2-diaminobenzene**

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

N,Nʹ-bis(2-hydroxybenzylidene)-1,2-diaminobenzene (HBDB) is prepared by irradiating a mixture of Salicylaldehyde (0.1mol) and o-phenylenediamine (0.05mol) in 2-3 ml of ethanol for about 3 minutes in a microwave oven. The resulting product was then recrystallized with methanol and ether and finally dried under reduced pressure over anhydrous CaCl₂ in a desiccators.

HBDB and the metal chloride were mixed in 1:1 (metal: ligand) ratio in a grinder. The reaction mixture was then irradiated by the microwave oven by taking 3 - 4 mL of ethanol as a solvent. The reaction was completed in a short time (6 - 9 min) with higher yields. The progress of the reaction and purity of the product was monitored by TLC using silica gel G (yield: 80% - 85%). The resulting product was then recrystallized with a mixture of methanol, ethyl acetate and ether. The structure of the compound was established by using physical, analytical and spectral data.

**Antimicrobial procedure**

**Screening of antibacterial activity**

**Bacteria tested**

Totally three bacterial strains were used throughout investigation. All the bacterial cultures and fungal cultures were obtained from Microbial Type Culture Collection (MTCC), Institute
of Microbial Technology, Chandigarh, India. The young bacterial broth cultures were prepared before the screening procedure.

**Preparation of inoculums**

Stock cultures were maintained at 4°C on slopes of nutrient agar. Active cultures of experiment were prepared by transferring a loop full of cells from the stock cultures to test tube of Muller-Hinton broth (MHB) for bacteria that were incubated without agitation for 24 hrs at 37°C and 25°C respectively. The cultures were diluted with fresh Muller-Hinton broth to achieve optical densities corresponding to 2.0 $10^6$ colony forming units (CFU/ml) for bacteria.

**Antimicrobial susceptibility test**

The disc diffusion method (Bauer et al., 1966) was used to screen the antimicrobial activity. *In vitro* antimicrobial activity was screened by using Muller Hinton Agar (MHA) obtained from Himedia (Mumbai). The MHA plates were prepared by pouring 15 ml of molten media into sterile petriplates. The plates were allowed to solidify for 5 minutes and 0.1% inoculums suspension was swabbed uniformly and the inoculums were allowed to dry for 5 minutes. The concentration of extracts is 40 mg/disc was loaded on 6 mm sterile disc. The loaded disc was placed on the surface of medium and the extract was allowed to diffuse for 5 minutes and the plates were kept for incubation at 37°C for 24 hrs. At the end of incubation, inhibition zones formed around the disc were measured with transparent ruler in millimeter.

**RESULTS AND DISCUSSION**

![Fig 1: Metal chelates of 4-methyl[(5'-naphthylazo-2'-hydroxybenzylidene)amino]benzene (1-4) [M(MNAB)$_2$(H$_2$O)$_2$], where M=Cu(II),Co(II),Ni(II) or Mn(II).](image-url)
Fig 2: Metal chelates of \(N,N'\)-bis(2-hydroxybenzylidene)-1,2-diaminobenzene (5-8)[M(HBDB)(H_2O)], where M = Cu(II)[M(HBDB)(H_2O)_2], where M = Co(II), Ni(II) or Mn(II).

Antimicrobial activity

Table 1: Antimicrobial activity for [M(MNAB)_2(H_2O)_2]complexes where M = Cu(II), Co(II), Ni(II) or Mn(II).

<table>
<thead>
<tr>
<th>ORGANISM</th>
<th>C</th>
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<td>K.aerogenes</td>
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<td>13</td>
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<tr>
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</table>

The antibacterial test was conducted for the organisms Lactobacillus, S.aureus and K.aerogenes for [Cu(MNAB)_2(H_2O)_2](1), [Ni(MNAB)_2(H_2O)_2](2), [Co(MNAB)_2(H_2O)_2](3), [Mn(MNAB)_2(H_2O)_2](4), and the results compared with the control. Higher results are seen for the organism S.aureus with [Cu(MNAB)_2(H_2O)_2]. For the other organisms also the same complex proves to be the highest and [Cu(MNAB)_2(H_2O)_2] alone gives higher results than control.

Fig 3: Antimicrobial activity of complex for S. aureus
The antimicrobial activity was conducted for the organisms *Lactobacillus*, *S.aureus* and *K.aerogenes* for [Ni(HBDB)(H$_2$O)$_2$] (5), [Cu(HBDB)(H$_2$O)] (6), [Mn(HBDB)(H$_2$O)$_2$] (7) and [Co(HBDB)(H$_2$O)$_2$] (8) and the results compared with the control. Higher results are seen for the organism *S.aureus* with [Cu(HBDB)(H$_2$O)]. But all the results are lower than the control value.

**Table 2: Antimicrobial activity for [M(HBDB)(H$_2$O)$_n$] complexes where M =Cu(II), Co(II), Ni(II) or Mn(II) ; n=1 (or) 2**

<table>
<thead>
<tr>
<th>S. No</th>
<th>Organism</th>
<th>Control (mm)</th>
<th>5 (mm)</th>
<th>6 (mm)</th>
<th>7 (mm)</th>
<th>8 (mm)</th>
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<tbody>
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<td>1</td>
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</tr>
<tr>
<td>2</td>
<td><em>S. aureus</em></td>
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<td>16</td>
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<td>11</td>
</tr>
<tr>
<td>3</td>
<td><em>K. aerogenes</em></td>
<td>18</td>
<td>11</td>
<td>11</td>
<td>10</td>
<td>11</td>
</tr>
</tbody>
</table>
Fig 6: Antimicrobial activity of complex for *Lactobacillus*

Fig 7: Antimicrobial activity of complex for *S. aureus*

Fig 8: Antimicrobial activity of complex for *K. aerogenes*
The chemistry of Schiff bases is a field that is being noticed. Schiff base ligands are considered privileged ligands because they are easily prepared by a simple one pot condensation of an aldehyde and primaryamines. These compounds and their metal complexes had a variety of applications including clinical, analytical, industrial they also play important roles in catalysts.

REFERENCES
