Research Article

Synthesis, DNA Binding, Cleavage and Antimicrobial Properties of Novel Mannich Base and its Metal Complexes

M.Sivakami1, B.Natarajan*, M.Vijayachandrasekar2, S.Rajeswari3, S.Ram Kumar Pandian4
1,2Department of Chemistry, SRM University, Kattankulathur, Tamilnadu, India.
3Department of Biotechnology, Kalasalingam University, Tamilnadu, India.
*Corresponding author’s E-mail: sivakamisudhasan@gmail.com

INTRODUCTION

Mannich reaction consists of amino alkylation of an acidic proton placed next to a carbonyl group with formaldehyde and ammonia or any primary or secondary amine. The final product is a β-amino carbonyl compound. Reactions between imides and aromatic aldehydes have also been considered as Mannich reactions. A review of literature regarding Mannich reaction shows extensive volume on chemical, biological and toxicological feature of Mannich bases, with vast applications as polymers, dispersants in lubricating oil and pharmaceutical agents. It is well known that compounds containing amide moiety as functional group have been found to possess donor properties and exhibit a wide range of biological activities. Transition metals are essential for normal functioning of living organisms and are, therefore, of great interest as potential drugs. The coordination chemistry of nitrogen donor ligands is an interesting area of research. A great deal of attention in this area has been focused on the complexes formed by 3d metals with bidentate ligands using both the nitrogen atoms of the substrates. The study of structural and binding features of various Mannich base complexes can play an important role in better understanding of the complex biological processes. Several drugs showed increased activity as metal chelates rather than as organic compounds. It has been reported in the literature survey, that Co(II) complexes with octahedral geometry show remarkable intercalative binding affinity as well as DNA cleavage properties. Further cobalt is an element of biological interest which is present in the active center of vitamin B12, which regulates indirectly the synthesis of DNA. It is known that there are about eight cobalt dependent proteins. Many cobalt complexes possess antitumor, ant proliferative, antimicrobial and antifungal activity. To the best of our knowledge no work has been done on this class of metal complexes with the Mannich base ligand SDMBTU. In the continuation of our research work, herein, we report the synthesis of a new Mannich base derived from succinimide, dimethoxy benzaldehyde and thiourea (SDMBTU) and the metal complexes with Mn(II),Co(II),Ni(II) and Cu(II). The characterization studies of all the metal complexes have been done with appropriate methods. All the metal complexes were screened for antibacterial and anti fungal activities. The DNA binding and cleavage studies of the cobalt complex containing the ligand SDMBTU is reported.

MATERIALS AND METHODS

All the reagents and solvents used for the synthesis of ligand and the metal complexes were Analar grade of highest available purity and used as such without further purification.

Physical measurements

Elemental analyses were performed using Carlo Erba 1108 analyzer and Coleman N analyzer and were found within ± 0.5%. The molar conductivities of the metal complexes were measured in approximately 10−3 M ethanol solution using a Systronics direct reading digital conductivity meter -304 with dip type conductivity cell. The IR spectra were recorded as KBr pellets on Perkin-Elmer 1000 unit instrument. Absorbance in UV-Visible

ABSTRACT

Succinimide (pyrolidine 2,5-dione) is a synthetically versatile substrate used for the synthesis of heterocyclic compounds and as a raw material for drug synthesis. Derivatives of succinimide are of important biological and pharmaceutical interest. Here the novel Mannich base 1-[(3,4-dimethoxyphenyl) (2,5-dioxopyrrolidin-1-yl)methyl] thiourea (SDMBTU) has been synthesized in good yield by condensation of equimolar quantities of succinimide, dimethoxy benzaldehyde and thiourea. Manganese (II), Cobalt(II), Nickel(II) and Copper(II) complexes of the above ligand have also been synthesized. Structures of newly synthesized compounds were confirmed by elemental analysis, IR, UV-VIS & NMR spectral studies. All the complexes adopt octahedral geometry around the metal ions. All the newly synthesized compounds were screened for their anti microbial activity against E.coli and B. subtilis bacteria by MIC technique. Anti fungal activity is also performed against Aspergillus niger, Candida albicans. Some of the compounds have shown marked activity against the selected micro organisms. The binding of the cobalt chloride complex of the ligand with calf thymus DNA has been investigated using absorption spectroscopy, fluorescence spectroscopy and viscosity measurements. The complex exhibits efficient nuclease activity.

Keywords: Anti bacterial, Antifungal, DNA binding and Cleavage, Mannich base.

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region was recorded in DMF solution using UV-Visible spectrometer. The \(^1\)H & \(^13\)C NMR of the ligand was recorded on a Bruker instrument employing TMS as internal reference and DMSO – DMF as solvent. The mass spectral study of the ligand was carried out using LC mass spectrometer. Magnetic susceptibility measurements at room temperature were made by using a Guoy magnetic balance. Anti bacterial activity has been carried out using MIC technique and antifungal activity is done by agar diffusion method.

**Anti-bacterial activity**

The ligand SDMBTU and the synthesized metal complexes were dissolved in DMSO and the working concentrations of the above were taken in Milli-Q water for treatment. Gram positive (Bacillus subtilis) and Gram Negative (Escherichia coli) bacteria were taken to analyze the anti-bacterial activity of metal complexes. Primarily, Minimal Inhibitory Concentration (MIC) was determined by spectrophotometer method. For that purpose, equal number of colonies (1x10\(^5\) CFU/ml) were taken in 0.7% of sterile saline and the final concentrations of metal complexes were varied from 50 µg to 400 µg. 12 hour incubation was given and absorbance was taken at 600 nm. 50% of reduction was calculated as MIC. Afterward, the activity of the drug was visualized by well-diffusion assay and the zone of inhibition was calculated.

**Anti-fungal activity**

To know the effect of ligand and the metal complexes against fungus, Candida albicans and Aspergillus niger were taken for analysis. Primarily, the activity was analyzed using well-diffusion method with the concentrations of 100 and 400 µg/ml. After, 24 hours of incubation the zone of clearance was observed.

**Scheme of Synthesis**

**Preparation of Mannich base 1-[(3,4-dimethoxyphenyl) (2,5-dioxopyrrolidin-1-yl)methyl] thiourea (SDMBTU)**

Succinimide, dimethoxy benzaldehyde and thiourea were taken in 1:1 molar ratio. In aqueous solution of succinimide and thiourea dimethoxy benzaldehyde was added drop wise and the mixture was stirred in a magnetic stirrer at room temperature for 8-10 hours. After a week a solid product formed was filtered, washed with distilled water, dried in an air oven at 60°C and recrystallized using ethanol and chloroform in 1:1 ratio. Figure 1.

**Mechanism**

The reaction route for the synthesis of Mannich base (SDMBTU) involves the condensation reaction of dimethoxy benzaldehyde with thiourea to form the imine product. This electron deficient imine then attacked by imide to give the ligand SDMBTU.

**Synthesis of metal complexes**

All the metal complexes of SDMBTU were prepared by slow addition of hot methanolic solution of the metal salt with hot ethanolic solution of the ligand in 1:1 molar ratio. The insoluble metal complexes were formed after 2 weeks. It was washed with methanol and ethanol to remove unreacted metal salt and ligand. The products were then dried in an air oven at 60°C. The proposed structures of the metal complexes are shown in Figure 2.

**RESULTS AND DISCUSSION**

**Physical properties & Elemental analysis**

The physical properties and elemental analysis of the prepared ligand and their metal complexes are described in Table 1. Structures have been suggested according to these data together with obtained from spectral analysis. The structure of metal complexes was further confirmed by conductivity measurements and magnetic moment determinations. Most of the metal complexes have been found to possess high melting points.

**UV-Vis Spectroscopic Studies**

The electronic spectra of the metal complexes were recorded for their solution in DMSO in the range of 180-1800 nm.

The UV-Vis spectrum of Manganese sulphate metal complex shows absorption bands at 18362 cm\(^{-1}\), 22457 cm\(^{-1}\) and 31293 cm\(^{-1}\) for \(^{4}\)A\(_{1g}\)→\(^{4}\)T\(_{1g}\), \(^{4}\)A\(_{1g}\)→\(^{4}\)T\(_{2g}\) and charge transfer transitions respectively. The \(\mu_{eff}\) value was found to be 4.998 B.M which suggests octahedral geometry\(^{27}\).

The electronic spectrum of Manganese chloride complex exhibits four absorption bands at 18050 cm\(^{-1}\), 24985 cm\(^{-1}\), 29125 cm\(^{-1}\) and 31272 cm\(^{-1}\) for \(^{4}\)A\(_{1g}\)→\(^{4}\)T\(_{1g}\), \(^{4}\)A\(_{1g}\)→\(^{4}\)E\(_{2g}\), \(^{4}\)A\(_{1g}\)→\(^{4}\)E\(_{1g}\) and charge transfer transitions respectively.
The μ_eff value of 4.85B.M points to a high spin octahedral geometry.28

The Cobalt sulphate complex shows four absorption bands at 6940 cm⁻¹, 14980 cm⁻¹, 18572 cm⁻¹, 24048 cm⁻¹ assigned for ²A_g→T₂g, ⁴A_g→T₁g, T₂g→T₁g and charge transfer transition. The μ_eff value was found to be 5.08B.M which agree with octahedral geometry.

The Cobalt chloride complex shows four absorption bands at 6703 cm⁻¹, 14365 cm⁻¹, 18742 cm⁻¹, 29066 cm⁻¹ assigned for ²T₁g→T₂g, T₁g→A₂g, A₂g→T₂g, T₁g→A₁g and charge transfer transition. The μ_eff value was found to be 4.48B.M which supports octahedral geometry.

The Nickel sulphate complex exhibits absorption bands at 10642 cm⁻¹, 16670 cm⁻¹, 23522 cm⁻¹ and 35714 cm⁻¹ due to ¹A₁g→3T₁g, ¹A₁g→3T₂g, ¹A₁g→3T₃g transitions respectively. The μ_eff value was found to be 1.48 B.M suggesting octahedral geometry.29

The Nickel chloride complex shows absorption bands at 10525 cm⁻¹, 15780cm⁻¹ and 24890 cm⁻¹ and 35235 cm⁻¹ for the transitions ¹A₁g→3T₁g, ¹A₁g→3T₂g, ¹A₁g→3T₃g and charge transfer transitions respectively. The μ_eff value was found to be 3.56 B.M suggestive of octahedral geometry.

For the sulphur complex of Copper appears at 8240 cm⁻¹, 11325 cm⁻¹, 14653 cm⁻¹, 26391 cm⁻¹ and 35670 cm⁻¹ due to ²B₁g→²A₁g, ²B₁g→²B₂g, ²E_g→²T₂g and CT transitions respectively. The μ_eff value was found to be 1.8 B.M in agreement with distorted octahedral geometry.

The copper chloride complex registers absorption bands at 927 cm⁻¹, 10374 cm⁻¹, 12357 cm⁻¹ due to ²B₁g→²A₁g, ²B₁g→²B₂g, ²E_g→²T₂g transitions respectively. The charge transfer transition bands occur at 24830 and 28327 cm⁻¹. The μ_eff value was found at 2.09 B.M suggesting octahedral geometry.

Table 1: Analytical data & UV spectral data of the ligand SDMBTU & its metal complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>C</th>
<th>H</th>
<th>N</th>
<th>O</th>
<th>A (cm⁻¹)</th>
<th>Transition Assignment</th>
<th>Geometry</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDMBTU</td>
<td>54.53</td>
<td>6.29</td>
<td>11.92</td>
<td>18.16</td>
<td>18.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MnSO₄.2H₂O.SDMBTU</td>
<td>34.35</td>
<td>4.42</td>
<td>8.01</td>
<td>30.51</td>
<td>4.99</td>
<td></td>
<td>Octa hedral</td>
</tr>
<tr>
<td>MnCl₂.2H₂O.SDMBTU</td>
<td>36.08</td>
<td>4.64</td>
<td>8.42</td>
<td>19.23</td>
<td>4.85</td>
<td></td>
<td>High spin</td>
</tr>
<tr>
<td>CoSO₄.2H₂O.SDMBTU</td>
<td>34.09</td>
<td>4.39</td>
<td>7.95</td>
<td>30.28</td>
<td>5.08</td>
<td></td>
<td>Octa hedral</td>
</tr>
<tr>
<td>CoCl₂.2H₂O.SDMBTU</td>
<td>35.80</td>
<td>4.61</td>
<td>8.35</td>
<td>19.07</td>
<td>4.48</td>
<td></td>
<td>Octa hedral</td>
</tr>
<tr>
<td>NiSO₄.2H₂O.SDMBTU</td>
<td>34.11</td>
<td>4.39</td>
<td>7.96</td>
<td>30.29</td>
<td>1.48</td>
<td></td>
<td>Octa hedral</td>
</tr>
<tr>
<td>NiCl₂.2H₂O.SDMBTU</td>
<td>35.82</td>
<td>4.61</td>
<td>8.35</td>
<td>19.08</td>
<td>3.56</td>
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<tr>
<td>CuSO₄.2H₂O.SDMBTU</td>
<td>33.80</td>
<td>4.35</td>
<td>7.88</td>
<td>30.00</td>
<td>1.8</td>
<td></td>
<td>Distorted Octa hedral</td>
</tr>
<tr>
<td>CuCl₂.2H₂O.SDMBTU</td>
<td>35.47</td>
<td>4.56</td>
<td>8.27</td>
<td>18.90</td>
<td>2.09</td>
<td></td>
<td>Octa hedral</td>
</tr>
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</table>
IR spectra

In order to study the binding mode of the ligand to metal in the complexes, the IR spectrum of the free ligand was compared with the corresponding metal complexes. Selected vibrational bands of the ligand and its metal complexes and their assignments are listed in Table 2. The IR spectrum of the free ligand exhibited a strong band at 1690 cm\(^{-1}\) which could be assigned to \(\nu(C=O)\) of the succinimide ring. A weak band around 3297 cm\(^{-1}\) could be attributed to stretching vibration of \(\nu(N-H)\) bond.\(^{30}\) Another strong band observed around 1392 cm\(^{-1}\) can be assignable to \(\nu(C=S)\) vibration mode. In the metal complexes, the band corresponding to \(\nu(C=O)\) of succinimide ring was shifted to lower frequency range suggesting the coordination of carbonyl group with the metal ion. There is no shifting of bands at 1400 cm\(^{-1}\) and 750 cm\(^{-1}\) indicating the absence of coordination of C=S group with the metal ion. The N-C-N stretching frequency of the ligand at 1472 cm\(^{-1}\) was shifted towards lower values in all the complexes, indicating the involvement of the nitrogen of thiourea in coordination to the central metal ion. The participation of oxygen and nitrogen in coordination with the metal ion is further supported by the new band appearance of \(\nu(M-N)\) around 420-425 cm\(^{-1}\) in the far infrared region.\(^{31,32}\)

\(^1\)H NMR Data (DMSO/TMS, 500.3 MHz)

The \(^1\)H NMR spectra of the ligand shows a multiplet at \(\delta\) 2.57 due to imide proton. The doublet for one proton at \(\delta\) 3.96 is assigned to OCH\(_2\) proton. A multiplet between 7.170-7.574 \(\delta\) is assigned for aromatic protons. The singlet for one proton at \(\delta\) 9.85 is assigned to amide -NH.

\(^13\)C NMR Data (DMSO/TMS, 125.7 MHz)

The number of signals of sharp peaks represents the number of carbons of the ligand which are not chemically equivalent. \(^{13}\)C NMR – 40.0, 60.36, 116.00, 119.23, 120.32, 126.73, 131.04, 139.62, 159.62, 172.66, 179.35.

LC Mass Data

Chemical Formula: C\(_{14}\)H\(_{17}\)N\(_{4}\)O\(_{4}\)S: Observed value m/z-323.37. Calculated value m/z - 322.75 (M-1).

Anti-bacterial activity of Mannich base

The minimal inhibitory concentration of ligand SDMBTU was found to be 300 µg for \(E\).\(coli\) and \(B\).\(subtilis\). The activity was higher rate when the growth inhibition was observed at 600 nm. But at low concentrations survival of bacteria was observed. The inhibitory effect was proved with well-diffusion method and cleared zone of inhibition was observed with Mannich base shown in Table 3. Based on the MIC, among nine metal complexes five metal complexes have shown good activity. The ligand SDMBTU has shown more activity compared with other metal complexes. The effect of metal complexes as anti-bacterial agents has been discussed in the literature.\(^{33}\) Although metal chelation with MnCl\(_2\), MnSO\(_4\), CoCl\(_2\), NiSO\(_4\) and NiCl\(_2\) had resulted similar anti-bacterial effect against \(Bacillus\) sp and \(E\).\(coli\) complexion of SDMBTU series resulted in enhanced inhibition. The decreased activity of other metal complexes is due to poor bioavailability as the result of decreased solubility upon complexation.

Anti-fungal activity

The results from well-diffusion assay confirmed that the ligand and the metal complexes have the potential to inhibit fungal growth. Many samples were shown the
inhibition against fungal growth. The inhibition zones were measured and compared with controls. At the concentration of 400μg/ml the metal complexes potentially increase the clear zone against the growth of the fungus. This demonstrates that Mannich base and the metal complexes have the anti-fungal activity shown in Table 3. The antifungal activity of each compound was compared with standard drug Fluconazole. Among the screened compounds, ligands with MnSO₄, CoCl₂, NiSO₄ and CuSO₄ have emerged as active against fungal strains. Mannich bases are physiologically active because of the molecule solubility in aqueous phase. Compared with other compounds, the Mannich base SDMBTU show cases its potential in reducing the growth of fungus.³⁴

Table 3: Diameter of inhibition against bacteria in millimeter (mm) and Antifungal activity of the ligand and selected metal complexes.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Anti-bacterial activity</th>
<th>Anti-fungal activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E.coli</td>
<td>B.subtilis</td>
</tr>
<tr>
<td>SDMBTU</td>
<td>2.0±0.2</td>
<td>1.9±0.3</td>
</tr>
<tr>
<td>MnSO₄ 2H₂O. SDMBTU</td>
<td>1.6±0.5</td>
<td>1.7±0.3</td>
</tr>
<tr>
<td>MnCl₂ 2H₂O. SDMBTU</td>
<td>2.5±0.1</td>
<td>2.3±0.2</td>
</tr>
<tr>
<td>CoCl₂ 2H₂O.SDMBTU</td>
<td>2.2±0.3</td>
<td>2.1±0.05</td>
</tr>
<tr>
<td>NiSO₄ 2H₂O.SDMBTU</td>
<td>1.8±0.4</td>
<td>1.7±0.2</td>
</tr>
<tr>
<td>NiCl₂ 2H₂O.SDMBTU</td>
<td>1.4±0.2</td>
<td>1.3±0.2</td>
</tr>
<tr>
<td>CuSO₄ 2H₂O.SDMBTU</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

DNA Binding

One of the most important approaches in the development of drugs and chemotherapy against some cancers, viral and parasitic diseases involve drugs which interact reversibly with DNA. Hence, syntheses of new metal complexes which can bind with specificity to DNA and bring about its cleavage are of importance in the development of new antitumor agents.³⁵

Electronic Absorption Spectra

The binding of CT-DNA with the synthesized Co(II) complex was studied using UV absorption spectral method.

The concentration of CT-DNA per nucleotide [C(p)] was measured by using its known extinction coefficient at 260nm (6600 m⁻¹cm⁻¹)10. Tris HCl-buffer [5mM Tris(hydroxymethyl) amino methane, pH 7.2.50mM NaCl was used for absorption and viscosity experiments.

Absorption titration experiments were carried out by varying the DNA concentration (0-100μM) and maintaining the metal complex concentration constant. Absorption spectra were recorded after successive addition of DNA and equilibration (approximately 10 minutes). Absorption titration experiments with CT-DNA show intense absorption peaks at 230 and 280 nm in the UV region of the complex due to inter ligand π-π* transition of the coordinated groups in the complex. On addition of increasing amounts of DNA to the complex, both of the two characteristic peaks decreased gradually with the maximum hypochromicity of 15% & 20 % respectively, suggesting the strong interaction between the complex and DNA. The observed data were then fitted into the following equation to obtain the intrinsic binding constant Kb.³⁶

\[
[DNA]/(ea - ef) = [DNA]/(eb - ef) + 1/Kb (ea - ef)
\]

Where, ea, eb, and ef are the apparent, bound, and free metal complex extinction coefficients respectively at 263 nm (Figure 3).

Figure 3: Electron absorption spectra

Fluorescence spectra

Fluorescence quenching experiments were performed with ethidium bromide bound DNA with increasing concentrations of metal complex to determine the extent of binding between the molecule and DNA. Ethidium bromide is an indicator for fluorescence quenching.³⁷ The quenching extent of fluorescence EB bound to DNA is used to determine the DNA binding strength of the metal complex. The fluorescence quenching curves of EB bound to DNA in absence and presence of the complex was monitored. The addition of the metal complex to EB bound to DNA has shown a reasonable reduction in emission intensity indicating that the complex is bound to DNA at the sites occupied by EB (Figure 4). The quenching plots indicate that the quenching of EB bound to DNA by the metal complex is in good agreement with the linear Stern-Volmer equation.

DNA Cleavage

The CT DNA electrophoresis experiment for the metal (II) complexes exhibit nuclease activity in the presence of H₂O₂. Control experiment using DNA alone (Lane 1) does not show any significant cleavage of CT DNA against H₂O₂.
The cleavage efficiency of the complexes compared with that of the control is due to their efficient DNA-binding ability. From the picture (lanes 2-7), it is evident that the complex cleaves DNA more efficiently in the presence of an oxidant (\(\text{H}_2\text{O}_2\)). This may be ascribed to the formation of hydroxyl free radicals. The production of a hydroxyl radical due to the reaction between the metal complex and oxidant may be explained as shown below.

\[(\text{Ligand}) \text{Co}^{2+} + \text{H}_2\text{O}_2 \rightarrow (\text{Ligand}) \text{Co}^{3+} + \text{O}_2 + \text{H}_2\text{O}\]

The \(\text{OH}^+\) free radicals participate in the oxidation of the deoxyribose moiety, followed by hydrolytic cleavage of a sugar phosphate back bone. Co(II) complex showed marked nuclease activity in presence of \(\text{H}_2\text{O}_2\) oxidant which may be due to the increased production of hydroxyl radicals. Control experiments using DNA alone did not show any significant cleavage of CT-DNA even on longer exposure time. From the observed results, we conclude that the complexes cleave DNA as compared to control DNA in the presence of \(\text{H}_2\text{O}_2\) (Figure 5). Probably this may be due to the formation of redox couple of the metal ions and its behavior. Further, the presence of a smear in the gel diagram indicates the presence of radical cleavage.  

![Figure 4: Fluorescence spectra](image)

**Figure 4:** Fluorescence spectra

![Figure 5: A) Co(II) complex have shown complete cleavage of DNA at 50µM concentration. At 30 µM concentration Co(II) complex has cleaved super coiled (Form I) DNA where as the linear (Form II) is clearly seen. 40 µM \(\text{H}_2\text{O}_2\), alone has not displayed any activity over DNA. B) Cleavage of super coiled \(\text{pBR322}(0.35ug)\) by Co (II) complex in presence of triacetate EDTA (TEA) buffer C: Control DNA (untreated sample);1: DNA with 30 µM \(\text{H}_2\text{O}_2\); 2:7-DNA + 40 µM \(\text{H}_2\text{O}_2\) + with 20 -70 µM concentrations of sample.](image)

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**Viscosity measurements**

Viscosity measurements are used to explore the binding modes of complex with DNA. Optical photo physical probes provide necessary, but not sufficient, clues to support a binding model. To further clarify the interactions between the complex and DNA, viscosity measurements were carried out. Viscosity measurements that are sensitive to length change are regarded as the least uncertain and the most critical tests of a binding model in a solution in the absence of crystallographic structural data. A classical intercalation model demands that the DNA helix must lengthen as base pairs are separated to hold the binding ligand, leading to the increase of DNA viscosity. In contrast, a partial intercalation ligand could bend the DNA helix, reduce its effective length and, in tandem, its viscosity.

**CONCLUSION**

In this paper coordination chemistry of a Mannich base ligand obtained from the reaction of succinimide, dimethoxy benzadehyde and thiourea is described. Mn(II), Co(II), Ni(II) and Cu(II) complexes have been synthesized using the above Mannich base ligand and characterized on the basis of analytical, magnetic and spectral data. The Mannich base coordinates through its thiourea nitrogen and oxygen of succinimide to the metal ion and acts as a neutral bidentate ligand. All the complexes exhibit octahedral geometry. The ligand and its metal complexes have shown significant antibacterial & antifungal activity. The Co(II) metal complex showed efficient DNA binding ability and the binding constant value is consistent with other typical intercalators. The nuclease activity of the synthesized Co(II) complex was effective which could induce scission of \(\text{pBR322}\) super coiled DNA effectively to linear form in presence of \(\text{H}_2\text{O}_2\) as oxidizing agent.

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