Synthesis, characterization and anticancer studies of Co (II), Ni (II) and Cu (II) complexes with Schiff base derived from 2-hydroxy-1-naphthaldehyde and 3-(1H-imidazol-1-yl) propan-1-amine

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Abstract: Synthesized and characterized by CoII, NiII and CuII complex has been elemental analysis, UV-Vis, FT-IR and thermal analysis binding of this CoII, NiII and CuII complex with calf thymus DNA was investigated by UV-Visible absorption, the intrinsic binding constants Kb of complex with CT-DNA obtained from UV-Vis absorption studies. Further, the in vitro cytotoxic effect of the complexes examined on cancerous cell line, such as human breast cancer cells (MCF-7).

Keywords: Co II, Ni II and Cu II complex, DNA interaction, Electrochemical studies and cytotoxicity activity.

I. INTRODUCTION

Multinary metal/non-metal complexes and cluster actively investigated by chemists and physicists as they often combine structural and physical characteristics of the formally underlying binary components, and thus allow for further fine-tuning of respective properties [1-8]. The attachment of organic substituent on the surface of such cluster further enhances the diversity. This way the formation of ternary cluster can also occur via metal atom caturing by suitable ligand donor, pockets, e.g., upon terminating the organic ligands with chelating group to form M@T-E cluster,[9] or aromatic ligands.[10-14]

Many complexes have been synthesized. This complex can bind to DNA in non-covalent modes such as electro state, intercalative and groove binding [15, 16]. Many useful applications of these complexes require that the complex bind to DNA through an intercalative mode with the legend intercalating into the adjacent base pairs of DNA. Varying the substitutive group of substituent position in the intercalative ligand can create some interesting differences in the space configuration and the electron density distribution of transition metal complexes, which will result in some differences in spectral properties and will be helpful to more clearly understand the binding mechanism [17-20].

Accordingly, we intend to report herein, the synthesis of Co (II), Ni (II), Cu (II), complex with 3-(1H-imidazol-1-yl) propan-1-amine ligand and characterization of complex was carried out by elemental analysis, IR, UV-Vis and Electrochemical studies. The complex has been determined by ESI-Mass spectrometer. The binding properties of this complex to CT-DNA have been carried out using different physic-chemical methods and the binding modes are discussed. Multinary metal/non-metal complexes and clusters have been actively investigated by chemists and physicists as they often combine structural and physical characteristics of the formally underlying binary components, and thus allow for further fine-tuning of respective properties.[21-25].

II. FT - IR AND ELECTRONIC ABSORPTION SPECTROSCOPY

Electronic absorption spectra of all the complexes (Figure. 6.1) consist an intense absorption band in the range 271-307 nm, which is attributed to intraligand $\pi \rightarrow \pi^*$ transition [26]. The complexes also exhibit a lower energy band in the range 318-385 nm due to ligand-to-metal charge transfer (LMCT) transition. The d-d bands observed at 645 nm for complex **10**are assigned as $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ (ν1), $\rightarrow {}^4A_{2g}(F)$ (ν2), and $\rightarrow {}^4T_{1g}(P)$ (ν3), respectively in an octahedral environment. The complex **11**also shows three electronic spectral bands at 623 nm attributed to transitions $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$(ν1), $\rightarrow {}^3T_{2g}(F)$(ν2) and $\rightarrow {}^3T_{1g}(P)$(ν3) [27-29]. The complex **3** exhibits two broad absorption bands at 654 nm, which are assigned to $^2B_{1g} \rightarrow {}^2B_{2g}$ and $\rightarrow {}^2Eg$ transitions suggesting a distorted octahedral geometry [31].

The IR spectrum of all complexes 10–12 (Figure. 6.2(a-c)) show a sharp band in the region of 1617-1632 cm^{-1} due to the presence of ν(C=N) [32] formed as a result of condensation reaction of various aldehyde, which confirms the

presence of Schiff's base in complex. All complexes have bands in the region of 3429-3096 cm^{-1} and 2932-2043 cm^{-1}, which can be assigned to C–H stretching vibrations. Further evidence of coordination of ligands with the metal ions is revealed by the band at 459-692 cm^{-1} assigned to the metal-oxygen (M–O) vibration in all complexes [33].

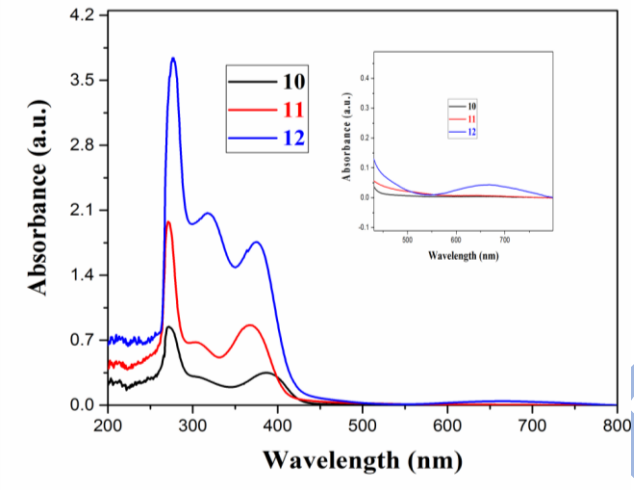
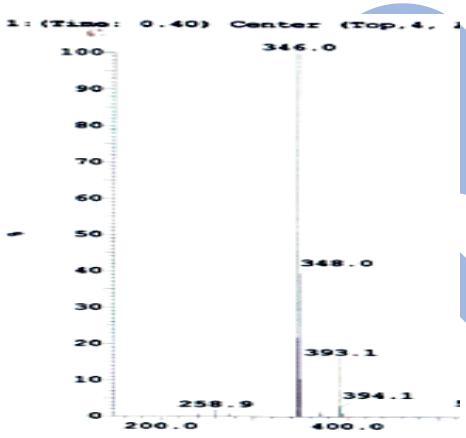
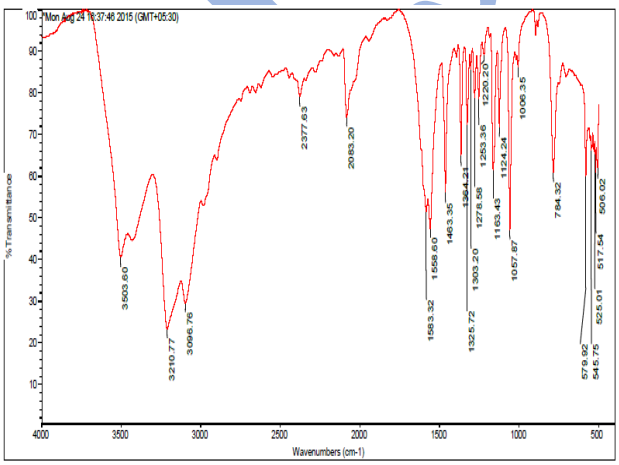
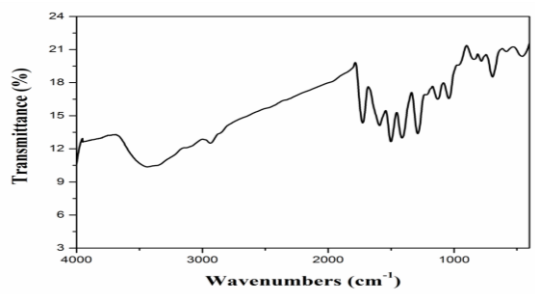


Figure.1. UV-Vis spectra of complexes 10-12.







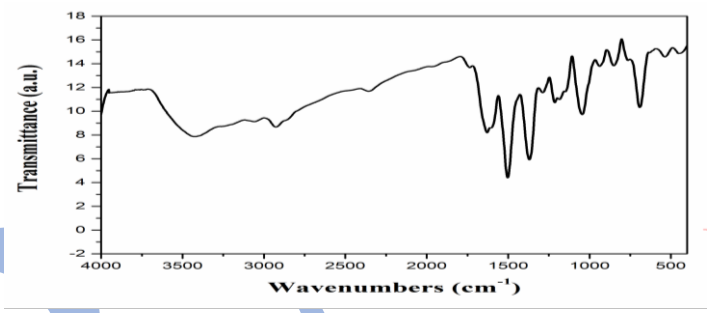


Figure.4. FT-IR spectra of complex 1-3.

Electrochemical studies

The electrochemical behavior of the complexes (10-12) (10^{-3} M) have been studied using cyclic voltammetry in the potential range of 0 to -1.2 V in the DMF solution containing 10^{-1}M tetra (n-butyl) ammonium perchlorate and scan rate 50 mVs^{-1}. The voltammograms of the complexes 10-12 were displayed in Figure. 6.3. The cyclic voltammograms of all the complexes 10-12 have almost the same shape, and exhibit one irreversible redox couple at 1.11, 1.5 for complex 10, 1.00, 1.44 for complex 11 and 1.10, 1.51 e V for complexes 12. ESI -mass (Figure. 6.4 (a-c)) and elemental analyses of complexes (10-12) are consistent with the proposed structure of complexes (10-12).

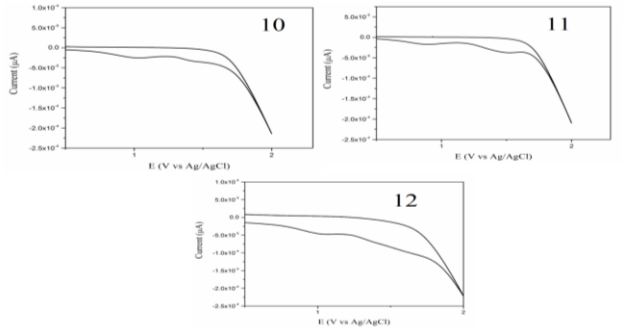


Figure. 5 Cyclic voltammograms of complexes 10-12.

III. DNA BINDING STUDIES

UV-Vis absorption titrations

The application of electronic absorption spectroscopy in DNA binding studies is one of the most useful techniques [34]. The absorption spectra of complexes 10-12 in the absence and presence of CTDNA (at a constant concentration of complex) was given in Figure. 6.5.

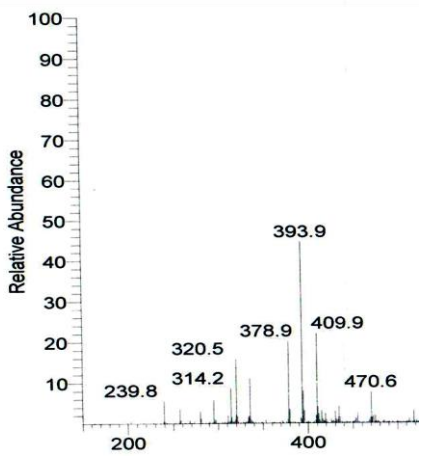
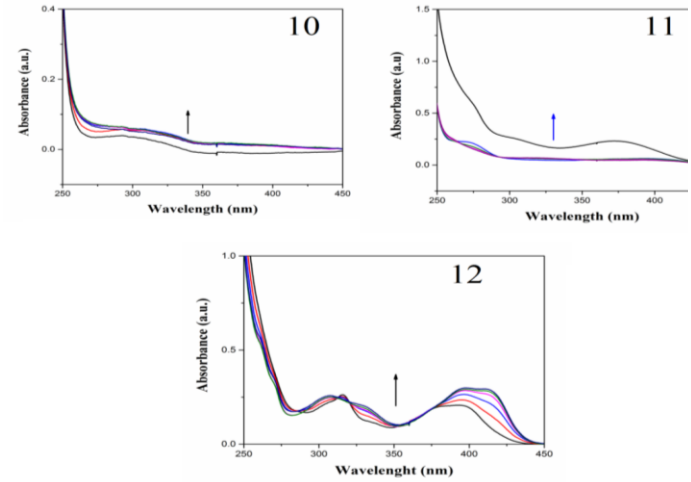


Figure.7. ESI mass spectrum of complex 1-3.

In the presence of DNA, the absorption bands of the complex 10 about 325 nm exhibited hypochromism of about 21% and with a red shift of 7 nm, 350 nm, 22% and blue shift of 3 nm for complex 11 and 390nm, 31% and blue shift of 5 nm for complex 12. The spectroscopic changes suggest that the complex has interaction with DNA. In order to affirm quantitatively the affinity of the complex bound to DNA, the intrinsic binding constants K_b of the complex with DNA was obtained by monitoring the changes in absorbance for the title complex with increasing concentration of DNA using the following Eq. [35-39]:

$$[DNA]/(\varepsilon_a - \varepsilon_f)=[DNA]/(\varepsilon_b - \varepsilon_f)+1/(K(\varepsilon_b - \varepsilon_f))$$

Where, [DNA] is the concentration of DNA in base pairs and the apparent absorption coefficient, ε_a, corresponds to A_{obs}/[compound]. ε_f refers to the extinction coefficient of the free compound and ε_b is the extinction coefficient of the compound when fully bound to DNA. The plot of [DNA]/(ε_a - ε_f) vs [DNA] gave a slope and intercept which are equal to 1/(ε_b - ε_f) and 1/K_b(ε_b - ε_f), respectively; K_b is the ratio of the slope to the intercept (Figure. 6.6).



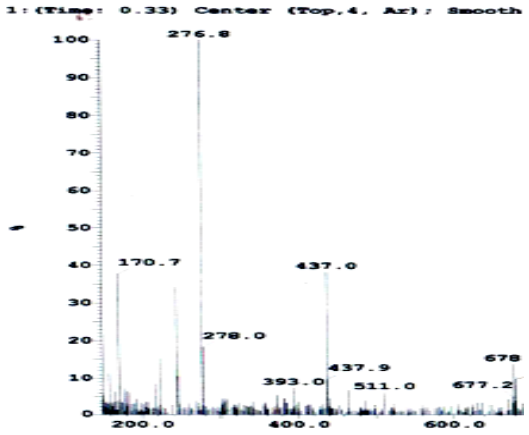


Figure.9. Absorption spectra of complexes (10-12) in 5 mM Tris-HCl/ 50 mM NaCl buffer upon addition of DNA. Arrow shows the absorbance changing upon increase of DNA concentration. The inner plot of [DNA/(εa-εf) vs [DNA] for the titration of DNA with complexes.

The λ_{max}, hypochromism, blue shift and binding constant values of all the complexes with CT-DNA indicate that there was a finite interaction between these complexes and CT-DNA. The observed K_b values have also revealed that the complexes bind to DNA via an intercalative mode [36].

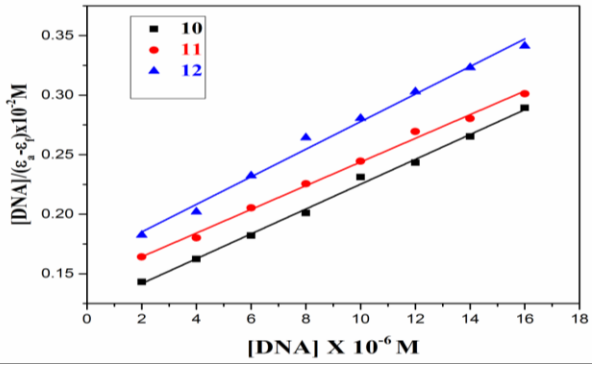


Figure.10. The plot of [DNA/(εa-εf) vs [DNA] for the titration of DNA with complexes(10-12).

The observed K_b value of complexes 10-12, 2.11 X 10^4, 2.15 X $10^4$and 3.11 X 10^4M^{-1}**,** respectively**.** This is expected as the incorporation of substitutent groups on aromatic ligand would hinder the insertion of the aromatic ring in between the DNA base pairs [40-44]. Thus, in general a planar extension of the intercalating ligand would increase the strength of interaction of the complexes with DNA Thus, the numbers of aromatic rings in the co-ligand and substitutent groups on aromatic ring dictate the DNA binding affinity and binding structure of the mixed ligand complexes. Though it has been found that the complexes can bind to DNA groove from the electronic absorption studies, the binding mode needed to be through some more experiments.

IV. CYTOTOXIC ACTIVITIES

Cytotoxic potential of newly synthesized complexes 10-12 were investigated on human breast cancer cell (MCF-7). The complexes (10-12) were applied in range of concentration 0.25-100 μM for MCF-7 and left for 48 h. The activities of the complexes were determined by MTT test in vitro and the results were expressed in terms of IC_{50} values. The relations of inhibition rates and complex concentration against human breast cancer cell (MCF-7) were shown in Figure. 6.14. The inhibition effects were further enhanced by increasing the concentration of complexes. At the concentration of 100 μM, inhibition rates of the complexes (10 and 11) against human breast cancer cells reached nearly same values and complex 12 is higher anticancer activities (IC_{50} value 23 μM). The values of IC_{50} for the complexes 10-12 were >100 μM. It is commonly believed that the biological activities of anticancer metal complexes are dependent on their ability to bind DNA and damage its structure resulting in the impairment of its function, which is followed by inhibition of replication, transcription processes and eventually cell death, if the DNA lesions are not properly repaired. The type of metal ion may be another reason for their different anticancer activity [45]. This is due to the fact that cobalt complexes have the capacity (Fig. 6.13) to reduce the energy status in tumours, as well as to enhance tumour hypoxia, which also influences their antitumor activities [46].

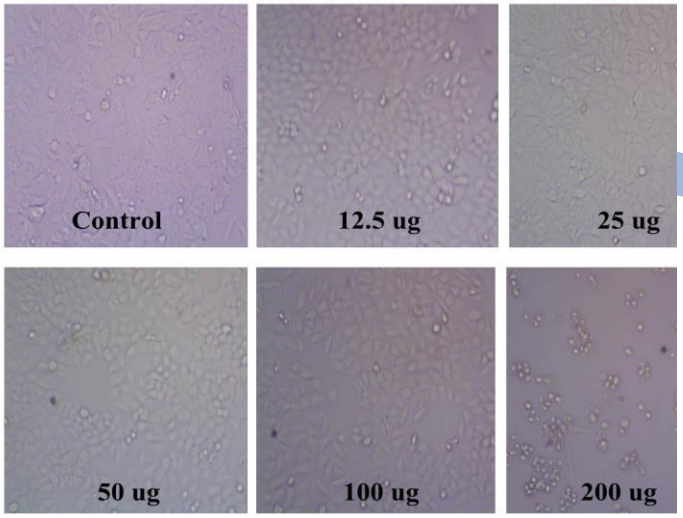


Figure.18. Cytotoxic effect of complexes (1-3) against MCF-7 at different concentration. Cell viability decreased with increasing concentration of complex 1.

V. CONCLUSION

In this work, we had synthesized and characterized copper (II) and nickel (II) Schiff's base complexes. We have carried out the electrochemical, DNA binding, antimicrobial studies of the synthesized complexes. It has been demonstrated that metal complexes with different Schiff base ligands can also be used as DNA and proteins binding and therapeutic agents. The synthetic versatility of the complexes permits wide tuning of their electrochemical and photo physical properties, and cytotoxicity activities. These advantageous aspects of metal complexes suggest a biological utility in applications, such as DNA interaction, are described. The present work would be helpful in the development of new therapeutic agents. These studies form an important rationale for drug design and warrant further *in vivo* experiments and pharmacological assays.

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