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Synthesis, Characterization and Interaction of Drug Based Cobalt (II) Complex with Herring Sperm DNA and Biological Activity

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Abstract: ***Novel complexes of copper (II), cobalt (II) and nickel (II) with sulphapyridine and aminothiazole were synthesized and characterized using spectral and analytical techniques. The interaction of cobalt (II) complexes with herring sperm DNA has been performed using absorption titration, viscometric measurements and cyclic voltammetry. The protective activity of metal complexes has been carried out using arose gel electrophoresis. The results indicate that cobalt (II) complex bind to DNA via electrostatic or groove binding with binding constant*** $K_b = 4.5 \times 10^4\ M^{-1}$***. The antioxidant activity for cobalt (II) complex was also checked.***

Keywords: hypochromism, peak potential and binding constant.

I. INTRODUCTION

The binding of metal complexes to DNA has been extensively studied over the past decade. Many coordination compounds are able to bind DNA as structural probes[1], DNA foot printing[2], DNA cleaving agents[3-4] and as potential anticancer drugs[5-6]. It is generally believed that many anticancer, antiviral, and antiseptic agents take action through binding DNA[4,7-8], since the interaction between small molecules and DNA can often cause DNA damage in cancer cells, blocking the division of cancer cells and resulting in cell death[9-11]. Many studies indicate that transition metal complexes can bind to DNA via both covalent (replacement of labile coordinating ligand by nitrogen base of DNA (i.e. adenine, Cytosine, guanine, thymine) and or non covalent interaction (intercalation, electrostatic or groove binding)[12]. Many important applications of these complexes require that they can bind via intercalative mode or groove binding [13]. Therefore interaction of complexes especially with planar aromatic heterocyclic ligands, which can insert into the base pairs of DNA duplex has attracted considerable attention[14-16]. is an essential element widely distributed in biological system[6,17-18]. Numerous cobalt complexes has been studied as hydrolytic agent for DNA cleavage[19-20], antitumor, antproli- ferative[21-23], antimicrobial[24-26] and antifungal[21,27], antiviral[28,29], antioxidant[12 ,30] and ant inflammatory activity[30]. They have exhibited antitumorogenic activity by reducing the number and size of carcinogen induced colon tumors and play synergistic role on the activity of certain antitumor drugs, although the mechanism has not been completely clarified[31-33]. Ligands having nitrogen donors received considerable attention because of their mixed hard-soft donor character, versatile coordination behavior [34-35] and for their biological activity (i.e., toxicity against bacterial growth [36], anticancer[37] and other biochemical properties[38]). The coordination geometry and nature of donor atoms play key roles in determining the binding extent of complexes to DNA. The importance of central metal ion at the core of the structure is noteworthy [39,40]. Many DNA heterocyclic compounds such as benzothiazole and benzopyra zine derivatives have been evaluated and found to be efficient intercalates [41-42].Antibiotics can interact with variety of biomolecules which may result in inhibition of the biochemical or biophysical processes associated with bio molecules[43]. There are number of antibiotics that require metal ion to function properly such as bleomycin, streptonigrin and bacitracin. Metalloantibiotics can interact with several biomolecules such as DNA, RNA, proteins and lipids making them unique and specially bioactive. The coordinated metal ion in these antibiotics play an important role in determining the proper structure and function of different antibiotics[44]. The transition metal ions are highly responsible for proper function of different enzymes. The activity of biometal is attained through formation of complexes with different bioligands and the mode of biological complexes depends upon the thermodynamic and kinetic properties. The lyophillicity of drug is enhanced through the formation chelates and the drug action is significantly increased due to the effective permeability of drug into the site of action. Interaction of various metal ions with the antibiotics enhance their antimicrobial activity as compared to that of free ligand [45] Many drugs in the form of metal complexes posses modified toxicological and pharmaceutical property. The results encouraged us to study the coordination chemistry of transition metal complexes and to study the binding behavior of cobalt(II) complexes with DNA and biological activity.

II. EXPERIMENTAL

A. Material and Method

All reagents, chemicals and solvents were of analytical grade and were used as such. Doubly distilled water was used throughout the experiment. Sulphapyridine, Aminothiazole, NaCl, DPPH, NBT, Ascorbic acid, Tris and herring sperm DNA (hs-DNA) were purchased from Sigma Chemical Company. Metal Chlorides (Copper Chlorides, Nickel Chloride and Cobalt Chloride) were purchased from E- Merck (India) Ltd. DNA stock solution was prepared by dilution of hs- DNA to tris buffer (containing 25 mM tris and 50 mM NaCl pH 7.2) followed by exhaustive stirring for three days and kept at 4 ^{0}C for no longer than a week. The stock solution of hs-DNA gave a ratio of UV absorbance at 260 and 280 nm (A_{260}/A_{280}) of 1.88, indicating that the hs-DNA was sufficiently free from protein contamination. The DNA concentration was determined by the UV absorbance at 260 nm after 1:20 dilution using $\varepsilon = 6600\ cm^{-1}$ [12].

IR spectra of the complexes were recorded on FTIR spectrometer with samples prepared in KBr pellets. Electronic spectra were recorded on Shimadzu UV 3600 Uv-Vis NIR spectrophotometer. The NMR spectra were obtained on Broker DRX 400 spectrometer operating at room temperature. Magnetic measurements were carried out on magnetic susceptibility balance of Sherwood Scientific (Cambridge U.K.) at room temperature. Elemental analysis was performed on Perkin Elmer 2408 elemental analyzer. Molar conductance was measured at room temperature on systolic Conductivity Bridge. Cyclic Voltammetry was performed SAS SP150 Biological Science Instrument carried out in 30 ml three electrode electrolytic cell. The working electrode was platinum disk, a separate pt single sheet electrode was used as counter electrode and Ag/AgCl electrode saturated with KCl used as reference electrode. KNO_3 and tris buffer was used as supporting electrolyte. The Cyclic voltammogram of the complex were recorded in tris buffer (pH= 7.2) at 100 mV/s. All electrochemical measurements were performed at room temperature. Viscosity measurements were carried out from the observed flow time of hs-DNA containing solution (t > 100) corrected for flow time of tris buffer alone (t_0) using Ostwald's viscometer at 25 ± 0.01^{0}C. Flow time was measured with a digital stop watch. Hydroxyl radicals generated by Fenton reaction were used to induce oxidative damage to DNA . The reaction mixture (15 µL) contained 25 mg of DNA in 20 mM phosphate buffer saline (pH 7.4) and 500 µg of test compounds were added and incubated with DNA for 15 minutes at room temperature. The oxidation was induced by treating DNA with 1 µl H_2O_2 30 mM, 1 µl 20 mM ferric nitrate and 1 µl 100 mM ascorbic acid and incubated for 1 h at 37 ^{O}C. The reaction was terminated by the addition of loading dye (40% sucrose and 0.25% bromophenol blue) and the mixture was subjected to gel electrophoresis [46] using Hi Media LA666 in 0.7% agarose/TAE buffer run at 100 V. DNA was visualized by Gel Doc system. The antioxidant activity was carried out using different assays. In DPPH (2,2-Diphenyl-1-picrylhydrazyl Diphenyl-1-picrylhydrazyl) assay quantitative measurement of radical scavenging properties of metal complexes were carried out according to the method by Blios et al [47]. Briefly 0.1 mM solution of DPPH was prepared in methanol and 1 mL of this solution was added to 3 mL of metal complex (100-300 µg/mL) and shikonin (300 µg/mL). α-tocopherol was used as a reference antioxidant. Discoloration of reaction mixture was measured at 517 nm after incubation for 30 minutes. The Superoxide anion radical scavenging activity involves measurement of scavenging activity of all the metal complexes based on the method described by Liu et al [48] with slight modifi- cation. 100µl riboflavin solution (20µg), 200µl EDTA solution (12 mM), 200µl methanol and 100 µl nitrobluetetrazolium (NBT) solution (0.1 mg/ml) were mixed in test tube and reaction mixture was diluted upto 3ml with phosphate buffer (50 mM). The absorbance of the solution was measured at 590 nm using phosphate buffer as blank after illumination for 5 minutes. Different concentrations (50 µl) i.e. 100 µg, 200 µg, 300 µg of complex solutions were used. Decreased absorbance of the reaction mixture indicates an increased super oxide anion scavenging activity. In hydroxyl scavenging activity-deoxyribose assay [49], the colorimetric deoxyribose (TBARS) method was applied as the reference method of comparison for determining the hydroxyl radical scavenging activity of metal complexes. The reacting mixture for the deoxyribose assay contained in a final volume of 1mL of the following reagents: 200 µL KH_2PO_4-KOH (100 mM), 200 µL deoxyribose (15 mM), 200 µL Ferric Chloride (500 µM), 100 µL EDTA (1 mM), 100 µL Ascorbic acid (1 mM), 100 µL Hydrogen peroxide (10mM) and 100 µL of complex (100-300µg/mL). Reaction mixtures were incubated at 37 ºC for one hour. At the end of the incubation period, 1 mL of 1% (w/v) thiobarbituric acid (TBA) was added to each mixture followed by the addition of 1 mL of 2.8% (w/v) trichloroacetic acid (TCA). The solutions were heated on a water bath at 80 ºC for 20 minutes to develop pink coloured malonaldehydethio- barbituric acid (MDA-TBA) adduct and the absorbance of the resulting solution was measured at 532 nm. In Ferric thiocyanate method (FTC) [50] 2 ml of complex solution (100-300 µg/mL) was mixed with 2.88 ml of linoleic acid (2.51%, v/v in 4 ml of 99.9% ethanol), 0.05 M phosphate buffer (pH 7.0, 8 ml) and distilled water (3.9 mL). The whole reaction mixture was incubated at 40 ^{O}C for 96 h. To 100, 300 and 400 µL of this solution, 9.7, 9.4, 9.3 mL of 75% (v/v) ethanol was added respectively followed by 0.1 mL of 30% ammonium thiocyanate. Precisely after three minutes, 0.1 ml of 3.5% v/v HCl was added to the reaction mixture, the absorbance at 500 nm of the resulting solution was measured and it was recorded again after 24 h, until

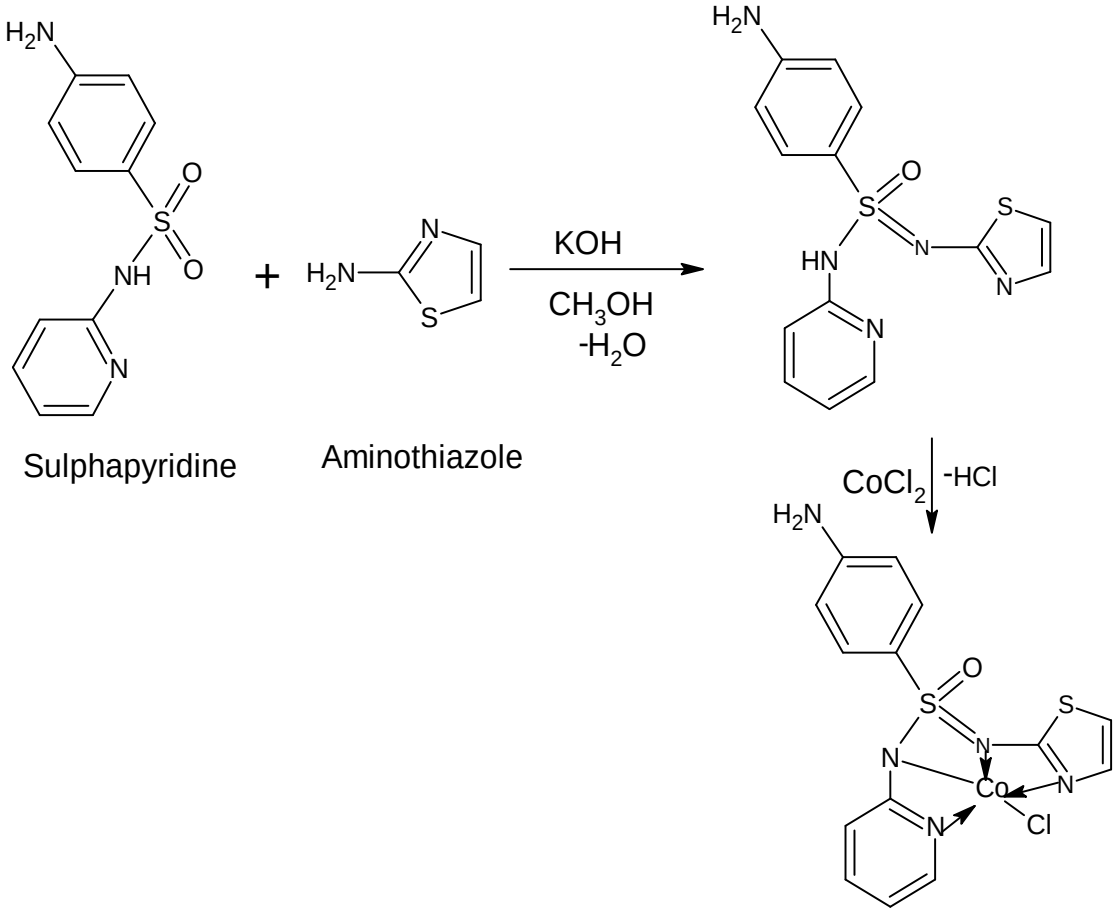
the day when the absorbance of the control reached the maximum value. α- tocopherol was used as reference antioxidant substance. In thiobarbituric acid assay, thiobarbituric acid was added to the reaction mixture which interacts with malanoaldhyde and TBARS produced was measured spectro photo metrically [51]. To 2 mL of reaction mixtures of ferricthiocyanate assay, 2 mL of TCA (20%) and 2 mL TBA (0.67%) was added and kept in boiling water for 10 minutes and were later on cooled under tap water. The reaction mixtures were centrifuged at 3000 rpm for 20 minutes and the supernatant was read at 500 nm. α- tocopherol was taken as reference antioxidant substance. The capacity to scavenge the radicals was calculated using the following equation:

$$\% \text{ inhibition} = A_c - A_s/A_c \times 100$$

Where 'A_c' is the absorbance of the controlled reaction (reaction mixture without any antioxidant substance) and 'A_s' is absorbance of reaction mixture with reference substance or complex. The experiments were repeated thrice.

B. General synthesis of complexes

A solution of sulphapyridine (2.49 g, 1mmol) and aminothiazole (1.00 g, 1 mmol) was refluxed in 50 ml absolute ethanol for ca 1h in presence of KOH. The reaction was monitored by TLC. To this solution was added cobalt chloride dropwise. A deep yellow precipitate was obtained, which was isolated from the hot solution washed with ether and dried in vacuo. Similar procedure was adopted for the preparation of Cu(II) and Ni(II) complexes. $C_{14}H_{12}N_5OS_2CoCl$: Yeild : 79%, Anal. (%Calcd./Found) C ; 39.59/39.63, H ; 2.84/2.87, N; 16.48/16.53. FT-IR (KBr, cm^{-1}); 3440 ν(NH2), 1571, 665, 433 ν(pyridine), 2920 ν(C-H),752 ν(C-S), 1330, $\nu(S=O)_{sym}$, 1145 $\nu(S=O)_{asym}$ 470 ν(M-N), 294 ν(M-Cl), μ_{eff} =3.69, soluble in DMF, DMSO. $C_{14}H_{12}N_5OS_2CuCl$: Yeild: 83%, Anal. (%Calcd./Found) C: 39.16/39.20; H: 2.81/2.85; N: 16.31/16.34; . FT-IR (KBr, cm^{-1}); 3443 ν(NH2), 1572, 652, 430 ν(pyridine), 2910 ν(C-H), 757 ν(C-S), 1335 $\nu(S=O)_{sym}$, 1151 $\nu(S=O)_{asym,}$ 476 ν(M-N), 300 ν(M-Cl) μ_{eff} = 1.75, soluble in DMF, DMSO. $C_{14}H_{12}N_5OS_2NiCl$: Yeild : 74%; Anal. (%Calcd./Found) C 39.61/39.64; H: 2.84/2.86; N: 16.49/16.52; . FT-IR (KBr, cm^{-1}); 3438 ν(NH2), 1571, 660, 435 ν(pyridine), 2918 ν(C-H),750 ν(C-S), 132 $\nu(S=O)_{sym}$, 1147 $\nu(S=O)_{asym}$ 474 ν(M-N), 304 ν(M-Cl) μ_{eff} = 2.62, soluble in DMF, DMSO.



Scheme 1 : General sequence for preparation of the complex

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III. RESULTS AND DISCUSSION

A. IR spectroscopy

The ir spectra of cobalt(II) complex displays a broad band due to v(NH_2) at 3440cm^{-1}. The characteristic bands of pyridine ring appear at 1570, 610 and 420 cm^{-1} respectively attributed to in-plane ring deformation and out of plane ring deformations[52-54]. Bands below 650 cm^{-1} are sensitive to coordination of pyridine through nitrogen to metal atom, as such band at 610 cm^{-1} and 420 cm^{-1} shift to higher energy by ca 55 cm^{-1} and 13 cm^{-1} respectively. The weak pyridine ring deformation at 1570 cm^{-1} is insensitive to coordination and remains unaltered. This type of coordination is also reported for other transition metal complexes[55-57]. The appearance of bands at 460-490 cm^{-1} and 280-320 are assigned to v(M-N) and v(M-Cl) respectively further confirming coordination through nitrogen atom[57]. Non involvement of sulphur is in accordance with earlier reports with various transition metal ions because sulphur is poor lewis base as compared to nitrogen[59].

B. Electronic Spectra

The absorption spectra of cobalt(II) complex were recorded in the range of 200-800 nm at 25^0 C in DMSO. The cobalt complex displays bands at 265 and 361nm assigned to LMCT transitions. The band at 560 nm due to the d-d transitions is characteristic of square pyramidal geometry for cobalt complex[60]

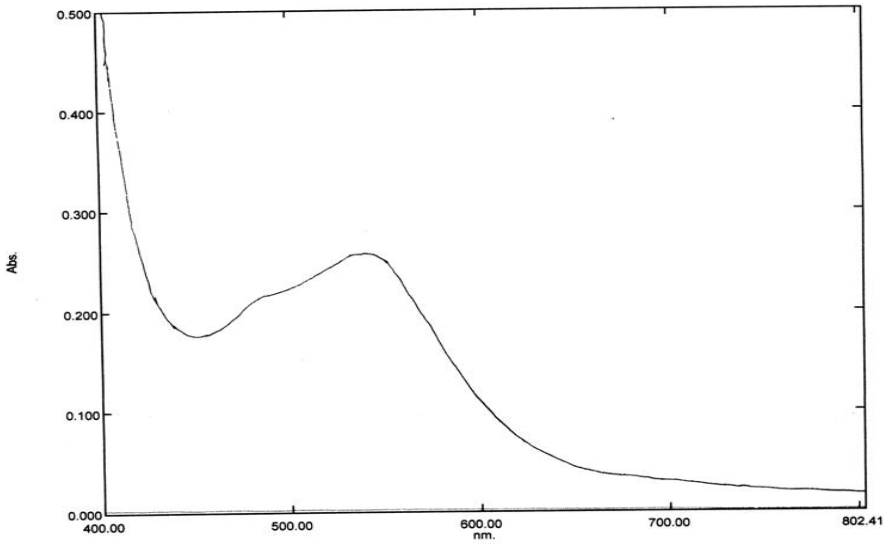

Figure 1. Electronic Spectrum of Cobalt(II) Complex.

The diamagnetic nickel (II) complex showed a broad band at 420 nm assigned to $^3B_1 \rightarrow {}^3E(F)$. The λ_{max} value is consistent with pent coordinate geometry around Ni (II) ion[61]. In addition the nickel(II) complex also exhibit bands at 313 nm assigned to LMCT transition. The copper (II) complex displays band at 310 and 340nm assigned to LMCT transitions and a d-d band at 773 nm, thus confirms the square pyramidal geometry for the complex.

C. Magnetic susceptibility studies

The magnetic susceptibility values for the copper(II) complex at room temperature lies in the range of 1.75 BM which corresponds to the one unpaired electron and are consistent with the d^9 configuration around copper(II) ion[62-63]. The magnetic susceptibility recorded for the cobalt(II) complex at room temperature is 3.69 B.M. Consistent with pentacordinated geometry.

D. EPR Studies

The X-band electron paramagnetic resonance spectrum of copper(II) complex was recorded under the magnetic field strength of 3000±1000 gauss using TCNE as field marker at liquid nitrogen temperature. The EPR spectrum exhibits $g_{\parallel}$ and $g_{\perp}$ values of 2.203 and 2.044 and g_{avg} = 2.097 calculated from the formula $g^2_{avg} = g^2_{\parallel} + 2g^2_{\perp}/3$. The values of $g_{\parallel}$ and $g_{\perp}$ are consistent with $d_{x^2-y^2}$ copper(II) ground state anticipated for square pyramidal geometry[64]. The g value is related to the axial symmetry parameter G, by the expression $G = (g_{\parallel}-2)/(g_{\perp}-2)$. The G value measures the extent of exchange interactions in polycrystalline solids. If G is greater

than 4 exchanges interaction is negligible and for value of G less than 4, considerable exchange interaction occurs. In the present case the value of G is 4.324, confirms that exchange interactions are absent in the complex.

E. NMR Spectra

The nmr spectra of the nickel(II) complex shows signal at 6.8 -7.16 ppm are attributed to the aromatic protons. The pyridine protons show multiplet at 7.3 – 8.06 ppm. The signal for NH_2 protons was observed at 5.6 ppm.

F. Electronic absorption spectral studies

The application of electronic spectroscopy is one of most useful technique in DNA binding studies[65]. Complex binding with DNA through intercalation usually result in hypochromism and bathochromism due to intercalative mode involving strong stacking interaction between aromatic chromophores and base pairs of DNA[66]. Hyperchromism has been observed for interaction of many drugs with DNA[67]. The hyper chromic effect might be ascribed to external contact (electrostatic binding)[68] or to partial uncoiling of helix structure of DNA exposing more bases of the DNA[69]. The metal complex can bind to double strand DNA in different binding modes on the basis of structure and type of ligand. As the double helix posses many hydrogen bonding sites which are accessible both in minor and major grooves, it is likely that imine group of metal complex form hydrogen bonds with DNA, which can contribute to the hyperchromism observed in absorption spectrum. The hyper chromic effect may also be due to the electrostatic interaction between positively charged cation and the negatively charged phosphate backbone at the periphery of the double helix DNA[70] However no red shift was observed in the absorption traces, which rules out coordinate binding with N_7 base moieties of DNA. The intrinsic binding constant K_b was calculated using the equation.

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

Where ε_a, ε_b and ε_f are apparent, bound and free extinction coefficient respectively. In the plot of $[DNA]/[\varepsilon_a-\varepsilon_f)$ vs [DNA], K_b is given by the ratio of slope to intercept. The binding constant for the complex is $5.4x10^4$ M^{-1}. From binding constant, it is quiet evident, that cobalt(II) complex binds strongly to the hs-DNA.

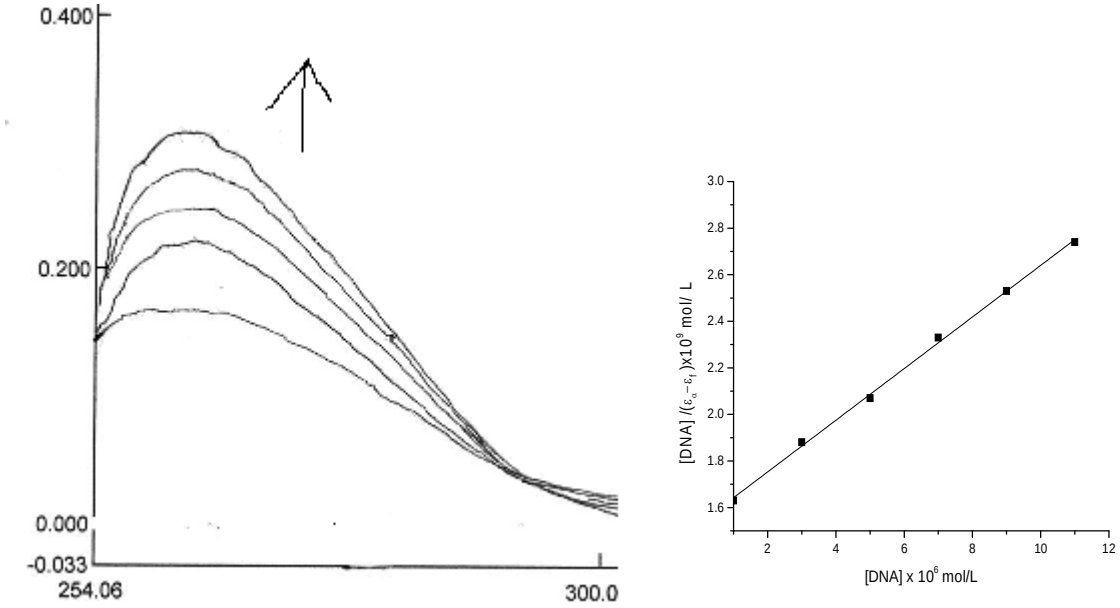

Figure 2. Electronic Spectra showing hyperchromicity. Figure 2a. Plot of $[DNA]/\varepsilon_a-\varepsilon_f$ versus [DNA] for absorption titration of hs-DNA with Cobalt(II) complex.

G. Cyclic voltametry

The application of electrochemical methods to the study of metallointercalation and coordination of metal ions and chelates to DNA provides a useful complement to previously used methods of investigation. Typical cyclic voltammetry behavior of cobalt(II) complex (0.1Mm) in absence and in the presence of hs-DNA are shown in figure. The cyclic voltammogram of Co(II) complex exhibits irreversible one electron redox process involving Co(III)/Co(II) couple at 0.419V. On addition of hs-DNA, cobalt(II) complex experienced a considerable decrease in voltammetric current coupled with a slight negative shift in formal potentials.

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Carter and coworkers [71-72] explained the drop of voltammetric currents in the presence of DNA can be attributed to the diffusion of the metal complexes bound to the large slowly diffusing molecule resulting a complex DNA product with a high diffusion affinity. However Kelly and coworkers [73] expounded another factor for the drop of peak currents. Complex bound to DNA and the product was non electro active, decreasing the concentration of electro active species in solution and resulting in drop of currents. In this case we found the drop of peak currents as well as negative shift of peak potentials and decrease of diffusion constant after addition of hs-DNA which can be attributed to the slowly diffusing complex-DNA compound. The more pronounced decrease of current upon addition of hs-DNA may indicate the binding affinity of cobalt(II) complexes to hs-DNA. The results corrobate the spectroscopic data.

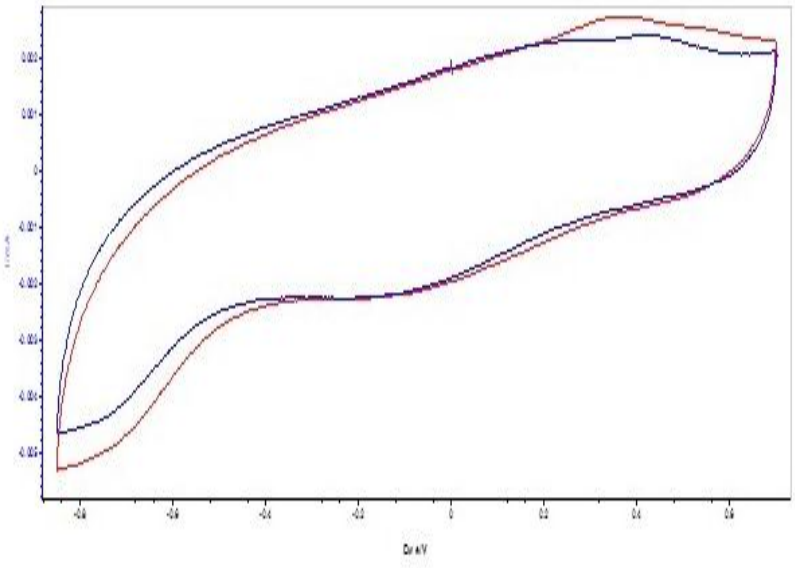

Fig. 3. Cyclic voltammogram of cobalt(II) complex in the presence and absence of hs-DNA.

H. Viscosity measurements

To investigate further the binding nature of complex to hs-DNA, viscosity measurements with solution of DNA incubated with cobalt(II) complex have been carried out. The viscosity of DNA solution is sensitive to the addition of metal complexes which can bind to DNA. While classical intercalative mode causes a significant increase in viscosity of DNA solution due to separation of base pairs at intercalation sites and increase in overall DNA length, complexes those bind exclusively in DNA grooves typically causes less positive or negative or no change in DNA viscosity [74]. The relative specific viscosity was calculated using the equation (t-to/t0) where to is the flow time for the buffer and t is the observed flow time for DNA in absence and presence of complex. The results were presented as η/η0 vs binding ratio [complex]/[DNA] where η is viscosity of DNA in presence of complex and η0 is viscosity of DNA alone (Fig). The relative specific viscosity of DNA decreased with increase in concentration of complex. The decrease in viscosity observed for the complex suggests hydrophobic interaction of complex with DNA surface encouraged by hydrogen bonding interactions leading to bending (kinking) of DNA chain.

I. Gel Electrophoresis

The chemical protectively activity of cobalt(II) complex was examined by gel electrophoresis. The principal of this method is that molecules migrate in the gel as a function of their mass, charge and shape. Binding of complex to DNA retards the movement of DNA under gel electrophoresis. The cobalt(II) complex retards the movement of DNA showing protectively activity. The reaction mixture was terminated by the addition of loading dye (40% sucrose and 0.25% bromophenol blue) and mixture was subjected to gel electrophoresis in 0.7% agrose / TAE buffer run at 100V. DNA as visualized by Gel Doc system is shown.

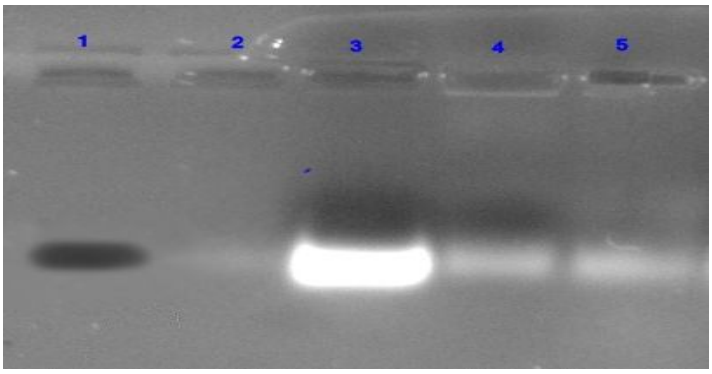

Figure 4. Lane 1: Native Calf thymus DNA + Reaction mixture; Lane 2: BHT + Reaction mixture + DNA; Lane 3: Native ct-DNA; Lane 4: Nickel complex (500 µg) + Reaction mixture + DNA; Lane 5: Cobalt(II) complex (500 µg) + Reaction mixture + DNA

J. Antioxidant activity

The antioxidant activity of metal complexes was compared with a positive control (BHT) and Ascorbic acid which is known to protect tissues and cells against various oxidative stresses[75], The mechanism of activity of scavenging of radicals cannot be evaluated by a single method, therefore five different antioxidant models were used in this study[76]. The antioxidant ability of the cobalt(II) complex is determined in the DPPH method by decrease in the absorption strength as indicated by discoloration (yellow colour) from original radical scavenging activities of cobalt(II) complex, Ascorbic acid, and BHT at 600µg/ml were observed to be 75%, 66% and 88% respectively (Fig.5). The cobalt(II) complex exhibited moderate superoxide dismutase activity at variable concentrations. The cobalt(II) complex exhibited higher scavenging activity (68%) at 150 µg/ml. However, BHT (75%) was found highly significant in scavenging the radicals (Fig.6).The hydroxyl radicals are known to cause DNA damage by degradation of deoxyribose moiety which contributes to carcinogenesis, mutagenesis and cytotoxicity[77], however, the scavenging or chelation of radicals by any substance is due to the antioxidant capacity of that particular substance[78]. In our study, cobalt(II) complex exhibits high chelating activity of hydroxyl radicals at a concentration range of 100–300µg/ml. Overall the scavenging activity decreased in the order of Ascorbic acid (83%) > BHT (65%) > Co(63%) at the concentration of 300 µg/ml (Fig.7). FTC evaluates the effect of a reference antioxidant and extracts on preventing peroxidation of polyunsaturated fatty acids and linoleic acid. The concentrations used were 100–300 µg/ml, percent inhibition was recorded after every 24 h and results are given here for three consecutive days. The percentage protective effect of linoleic acid peroxidation was 72% for cobalt(II) complex(Fig. 8). In the TBA method, formation of malanoaldehyde is the basis for evaluating the extent of lipid peroxidation. At low pH and high temperature malanoaldehyde, the end product of lipid per oxidation binds TBA to form a red colored complex. The concentrations used were 100–300 µg/ml. The FTC method measures the amount of peroxide produced during the initial stage of lipid peroxidation, subsequently at later stages of oxidation peroxides decompose to form carbonyl compounds that are measured by the TBA method. At concentration of 300 µg/ml the cobalt(I) complex exhibited 66% inhibition of radicals (Fig.9). Some of the reports mentioned the ferric reducing power of bioactive compounds such as phenolic substances and flavonoids [79-81]. The findings of this work confirm that cobalt(II) complex can be used as an alternative for the performing the various biological activities to combat various indigenous as well as exogenous stresses.

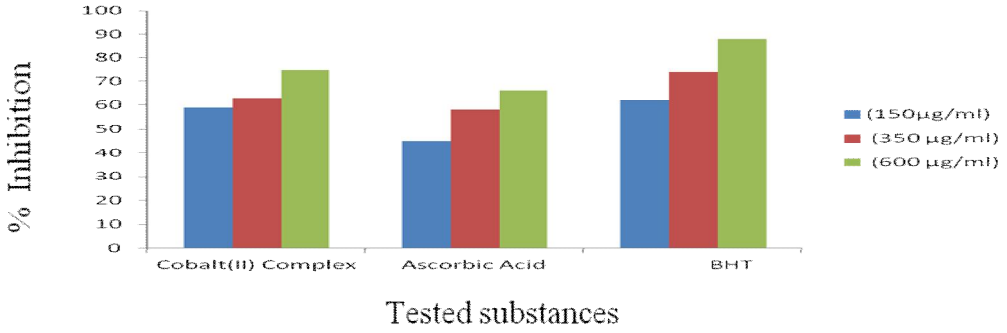

Figure 5

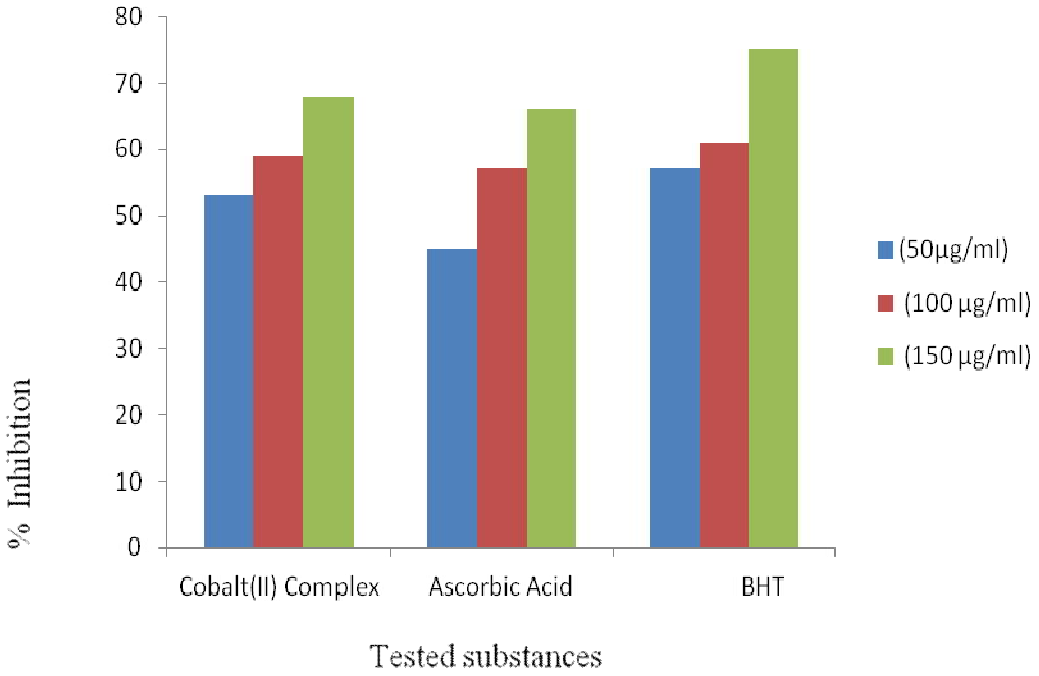

Figure 6

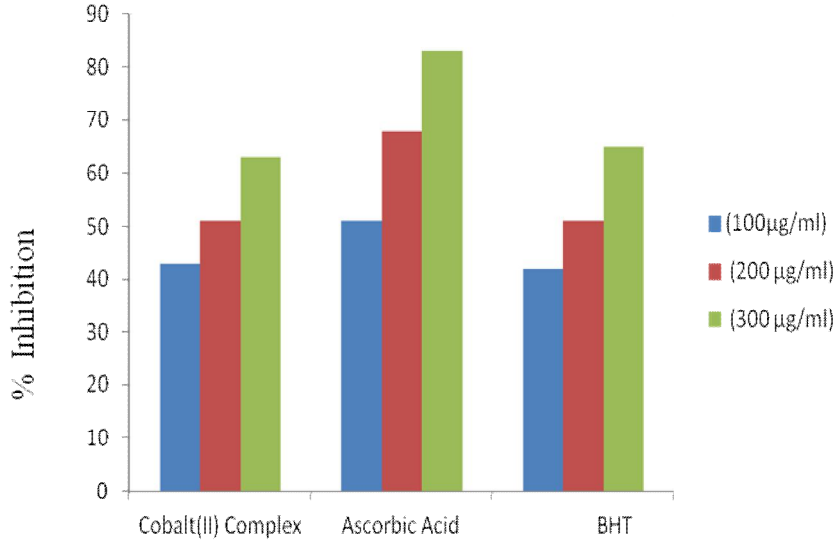

Figure 7

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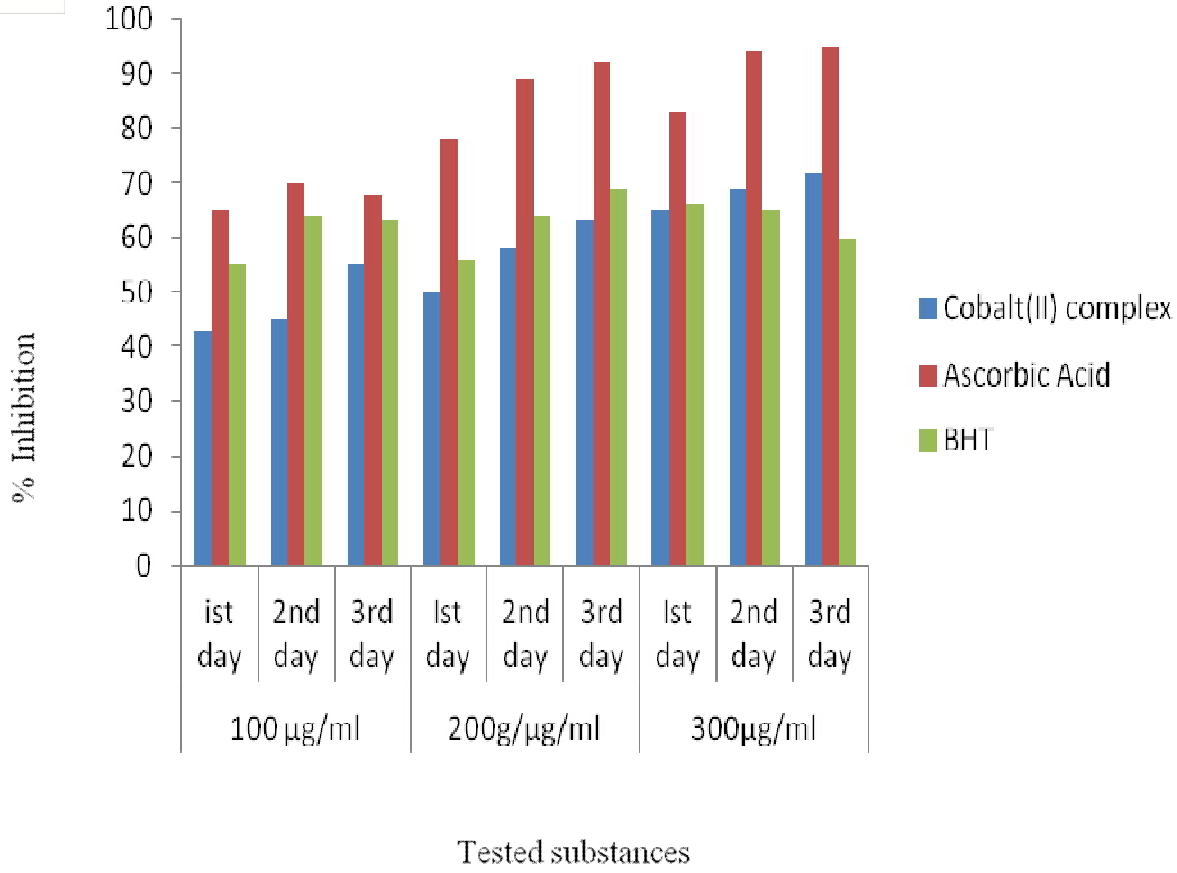

Figure 8

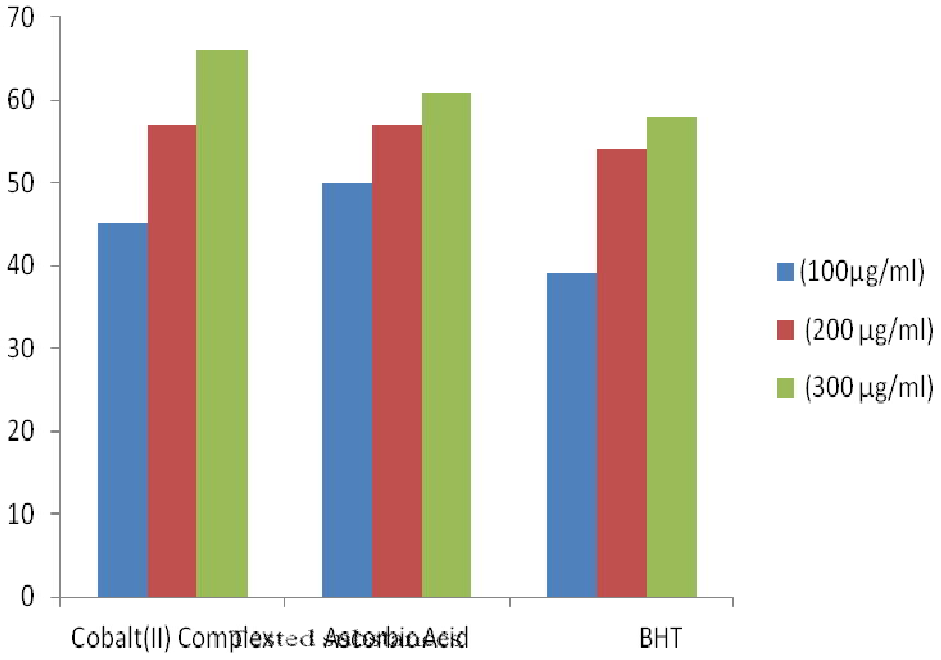

Figure 9

Table 1. IC_{50} determination of Cobalt(II) complex

	IC_{50} µg/ml				
Complexes	DPPH assay	SOD	Hyrdoxyl scavenging assay	FTC	TBA
Cobalt(II) complex	160	80	180	175	180
ASCORBIC ACID	175	60	>300	70	100
BHT	117	40	97	70	160

IV. CONCLUSIONS

In summary the metal complexes derived from aminothiazole and sulphapyridine were synthesized and characterized by various physicochemical methods. The interaction of cobalt(II) complex with hs-DNA was studied by absorption spectroscopy, viscosity and cyclic voltammetry under physiological conditions. The protectively activity was studied by gel electrophoresis. The results reveal that cobalt(II) complexes is capable of binding to DNA via electrostatic or groove binding mode and show considerable DNA damage protective effect. The cobalt(II) complex was also studied for antioxidant activity using different assays and the results reveal strong antioxidant activity. Thus the metal complex derived from sulphapyridine and aminothiazole posses strong potential to be used as possible therapeutic agent.

V. ACKNOWLEDGEMENT

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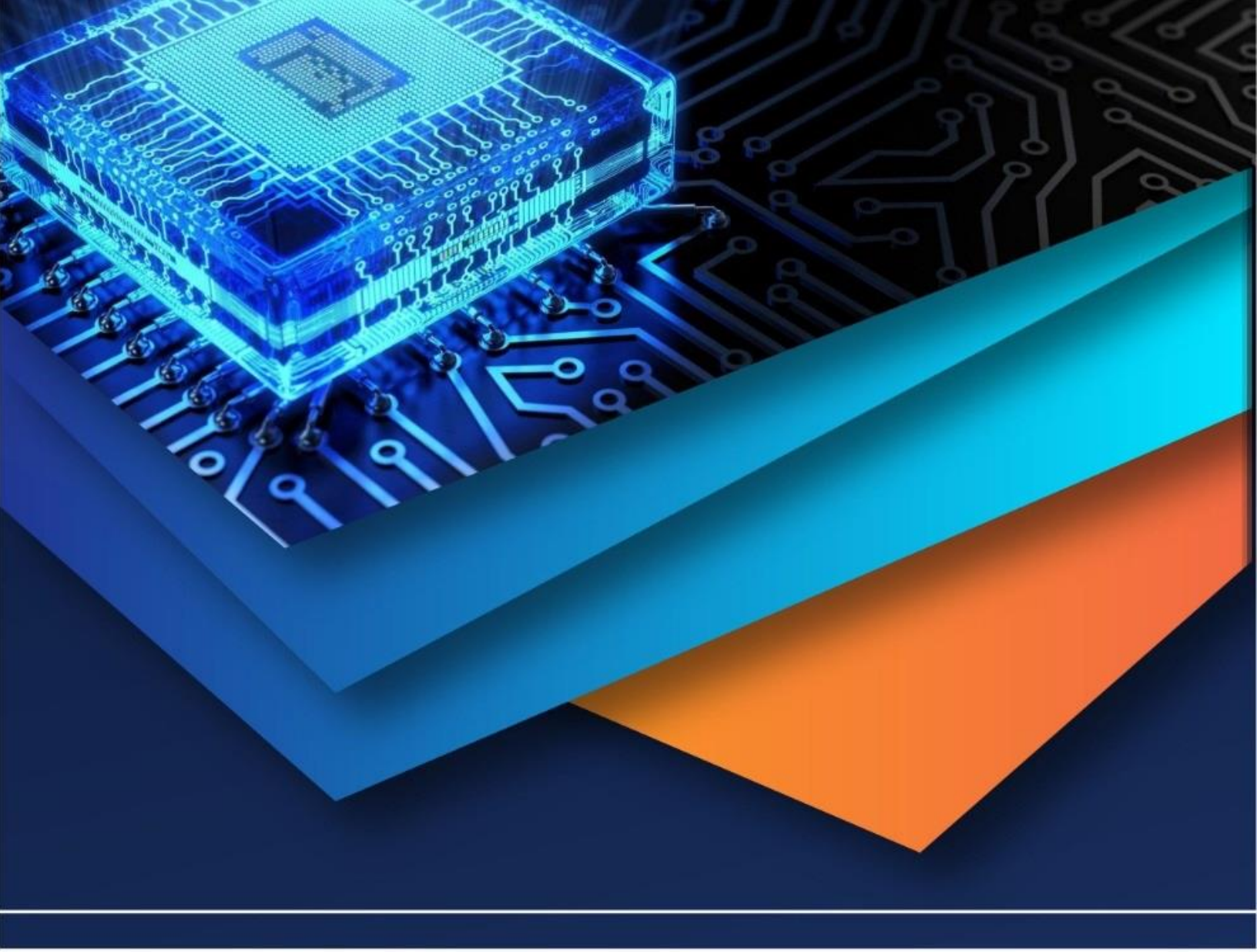

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