Co (II), Ni (II) and Cu (II) metal compounds of 2-aminonicotinaldehyde: Synthesis, crystalline structure, pharmacological assessment, and molecular docking research are all part of the process.

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Abstract

The ligand 2-aminonicotinaldehyde (2-ANA) and metal compounds of [Cu(2-ANA)2Cl_2], [Ni(2-ANA)2Cl_2], and, [Co(2-ANA)2Cl_2] have synthesis and research by using analytic and spectroscopical techniques (UV, IR,1H-NMR and Mass). The 2-ANA and [Co(2-ANA)$_2Cl_2$] complex single crystal X-ray diffraction experiments have been describe. Both compounds have intra/intermolecular hydrogen bonding, and the N-particle of the pyridine ring of 2-ANA is tetrahedrally coordinate to M-ion. Molecular docking research for microbiological examination, antioxidants, in antibacterial activity, and EGFR target were performed on metal chlorides, 2-ANA, and their complexes, which revealed that metal complexes have a synergistic effect on biological activity when compared to liberal ligand and M-Cl.

Keywords: Metal compounds; inter or intra molecular H-bonding; tetrahedrally; interactivity impact. 2-aminonicotinaldehyde (2-ANA); metal compounds; intra or inter particles H-bonding; tetrahedrally; interactivity influence.

1. Introduction

M-organic categorization, crystal development of technology [1], non-linear optic materiel [2-4], therapeutic [5], and catalytic nature of research [6] have all emerged as new areas of modern coordination chemistry in recent years [7]. Several classes of ligands have been produced over time for use in various uses [8-13].

Each category of ligand structure develop from 2-aminoaldehydes was widely use as construction pigmentation for black Orlon [14], as well as a number of biologically relevant compounds including such naphthyridine chemical compounds as antimutagenic, pain relievers [15], and anti-cancer activity [16]. The Co (II) compounds of nicotinaldehyde has recently been discovered to be an effective specific inhibitor of nicotinamidases, the metabolism enzyme leads to the development and pathogenisity of various pathogen micro-organisms [17]. Furthermore, the constant H-bonding motif has important applications in morphologic chemistry and molecular device, such as in the oxygen carrying conversion of haemoglobin and the morphologic nature of DNA molecules. Hard or weak, inter or intra molecule H-bonding provide an unusual supramolecular stacking structure in the solid state of 2-ANA and [Co(2-ANA)$_2$Cl$_2$] complex[18]. 2-ANA's stability and coordination chemistry differed significantly from those of its counterpart, 2-aminobenzaldehyde [19], are three possible co-ordination particles such as N atom of the pyridine ring (P-R)[20], which is the highly likely electron donor nature, and the another are the N-particle in amine and the O atom in aldehyde. Furthermore, previous research has shown that 2-ANA and parallel has been use to generate different M-compounds in which the N atom of the P-ring is linking to the M-ion [21]. The versatility of amino-aldehydes as ligands, as well as a possibility of have many possible metal interaction sites in ligand and constant intra or inter molecule H-bonding, prompted as to examine co-ordination capabilities of 2-ANA. We describe the preparation of 2-ANA and M-compounds with Co (II), Ni (II), and Cu (II) ions in this context. IR, ^{1}H-NMR, ^{13}C-NMR, and UV-region data were use to describe these compounds. ANA and the [Co(2-ANA)$_2$Cl$_2$] complex were study by using single crystal X-rays. The presence and different of hard/soft H-bond networks in 2-ANA and [Co(2-ANA)$_2$Cl$_2$] complexes were discovered through crystal structure research. Selected microbes were investigated in vitro for antimicrobial properties versus two gram-positive pathogens, B. subtilis and S. aureus, as well as two gram-negative pathogens, K. pneumoniae and E. coli, and in antifungal activity against A. niger and P. notatum. Antioxidant and anti - inflammatory effects of the compounds were also investigated [22].

2. Experimental

2.1 Materials, procedures, and apparatus

All of the compounds employed were of synthetic quality. The solution was cleansed correspondingly to industry standards. E.Merck provided us with metal salts (India). The melting point was determined with B.Electro-thermal melting point equipment, and the elements analysis was performed, at room temperature, the ^{1}H and ^{13}C-NMR data as acquired on Bruker Ascend-425 MHz analyzer using DMSO-D6 as component. The internal standard used to record these spectra was tetramethylsilane (TMS). TGA was carried out on a NETZSCH STA-2500 Regulus thermal polarizer in an N environment (RT-725°C) at 15-18°C/ minutes, by distributing the solid materials as KBr or Nujal mulls, FTIR spectra (3680-180 cm^{-}

[1]) was acquired on a PE 100S spectra[23, 24]. The IR spectrum of the ligands and M-compounds is measure in the region of 225-785 nm by using a JASCO V-670 SP-meter. The amount of M-Cl in the sample was assessed using a conventional technique [25].

2.2 The chemicals are synthesis

2.2.1 2-ANA synthesis

The ligand 2-ANA was produced using the process described previously and Yellow crystals appropriate for X-ray method was acquire by using re-crystallization from ethanol. 30 % yield C, 55.83; H, 3.95; N, 21.82. Anl. Cal. for $C_6H_6N_2O$%: C, 56.84; H, 3.89; N, 23.73. C was 58.81, H was 4.83, and N was 22.87. 3414 (N-H), 1655 (C=O), 1565 (C=N) (Pyridine) IR (KBr, cm-1) (M.P. 96.0 C). 9.78 (s, ^{1}H), 7.15 (d, J = 7.0 Hz, ^{1}H), 7.00 (d, J = 7.0 Hz, 1H), 7.34 (s, 2H, -NH2), 6.81-6.84 (s, 2H, -NH2), 6.60-6.63 (s, 2H, -NH2), 6.63-6.66 (s, 2H, -NH2), 6.62-6.65 (s, 2H, -NH (m, 1H). ^{13}C-nmr (DMSO, ppm, 100 MHz): δ 189.11, 157.60, 148.16, 143.03, 111.41, and 113.67.

2.2.2 Synthesis of [Co(2-ANA)$_2$Cl$_2$], 1

Synthesize compound of 2-ANA (0.471 g, 3.90 mmol) dissolve in 25 ml CH_3OH and $CoCl_2.4H_2O$ (0.425 g, 3 mmol) dilute in 12 ml ethanol was mixed at ref. tem. for about 3.30 hours. High ethanol was remove in vacuum at the end of the reaction and after cooling, filtered, to produce 71% compound. Anl. Cal. for [$Co(C_6H_6ON2)_2Cl_2$] (%): c, 39.58; H, 4.25; N, 12.51. Find: C, 35.63; H, 3.26; N, 13.44. m.p.298 ˚C (deco.); Ir (KBr, cm^{-1}): 3323 ($\upsilon_{(N-H)}$), 1674 (υ(c=0)), 1562 ($\upsilon(c_{=N})$ ($_{Py}$)). ^{1}H-NMR (DMSO, ppm, 425 MHz): δ 8.52 (s, 2H, -CHO), 7.89 (d, J = 8.0, 2H), 8.84 (d, J = 8.0, 2H), 8.31 (s, 4H, -NH_2), 5.62-5.65 (m, 2H). ^{13}C-NMR (DMSO, ppm, 100 MHz): δ 191.11, 155.45, 153.25, 143.07, 113.48, 114.81.

2.2.3 Preparation of complex [Ni(2-ANA)2Cl2], 2

Complex two is made in the same way. Result of compound [$Ni(C_6H_6ON_2)2Cl_2$] 66%. Anl. Cal. for [$Ni(C_6H_6ON_2)_2)Cl_2$]percentage); C, 31.44; N, 11.69; H, 3.21. Find: C, 31.81; N, 11.90; H, 3.48. mp.313 ˚C; ir (KBr, cm^{-1}): 3465 ($\upsilon_{(N-H)}$), 1645 (υ(c=0)), 1560 ($\upsilon(c=_N)$ (Pyridine)). ^{1}H-NMR (DMSO, ppm, 300 MHz): δ 8.81 (s, 2H, -CHO), 8.98 (d, J =8.0, 2H), 8.12 (d, J = 8.0, 2H), 7.34 (s, 4H, -NH_2), 7.52- 6.56 (m, 2H). ^{13}C-NMR (DMSO, PPM, 110 MHz): δ 183.57, 147.98, 144.15, 134.84, 102.85, and 107.71.

2.2.4 Complex [Cu(2-ANA)2Cl2] preparation, 3

Compound 3 is made in the same way1. Result of compound [$Cu(C_6H6ON_2)2Cl2$] 68%. Anl. Cal. for [$Cu(C_6H_6ON_2)_2Cl_2$](percentage): C, 27.85; N, 12.14 H, 3.45; Find : C, 25.79; N, 9.95; H, 2.45. mp.141 ˚C; ir (KBr, cm^{-1}): 3432 (υ(N-H)), 1661 (υ(c=0)), 1552 (υ(c=N) (Py)). ^{1}H-nmr (DMSO, PPM, 300 MHz): δ 9.64 (s, 2H), 9.37 (d, J = 7.2, 2H), 7.05 (d, J = 7.4, 2H), 8.54 (s, 4H, -NH2), 7.64-7.69 (m, 2H). ^{13}C-nmr (DMSO, PPM, 100 MHz): δ 192.67, 157.21, 153.85, 144.92, 112.56, and 113.24.

2.3 Crystal structure determination

Ethanol liquid slowly evaporating, solitary ligand crystals (2-ANA) and $[Co(2\text{-}ANA)_2Cl_2]$ compound, appropriate for X-ray data investigation, was produced, the SAINT programme was use to help with data integration and reduction. Using the tool SADABS, the data will be subjected to multiscan empirical absorbency adjustments. Structures was solve by using direct and polished on F2 using the SHELXL–97 programme, which used full–matrix least squares. Anisotropic refinement was used on all non-hydrogen atoms. The hydrogen atoms were found and refined using Fourier mapping [26-31].

2.4 Investigations into bio-assays

2.4.1 Antimicrobial properties

The disc diffusion method was used to test the antimicrobial properties of the 2-ANA as well as transition metals versus two punnet pathogens (Bacillus cereus, S. aureus), two punnet microorganisms (E. coli, and, K. pneumonia), and two fungal strains (P.notatum, and, A.niger). Sterile conditions antimicrobial discs with a diameter of 5 mm have been used put over the nutritional agar material by using Whitman (No. 1) paper. 100 g/mL conc. chemicals was apply to disc using a micropipette (complexes was initially dissolve in DMSO); micro-organism and fungus was then cultured at 38°C and 26°C. The inhibitory area was measured in millimeters, identified by using conventional medicines. Antibiotic 28 g/disc (std. medicines) and std. Antibacterial medication Occur in a range (8g/disc) was utilize as DMSO was used as a zone of inhibition, whereas objective of ensuring were used, all experiments was done in the mean isolate, or the (MIC) estimates for the investigated drugs and references in g/mL, was collected in carried out in triplicate.

2.4.2 Antioxidant properties

Using the DPPH free radical technique reported in literature, the ability to scavenge free radicals of ligand 2-ANA and metal compounds was tested [32-34]. A scorbic solution, which was employed a control, in 100% methanol, a 0.2 mM DPPH solution was produced. The test chemicals was dissolve in 0.3 percent DMSO and CH_3OH to make 1 mM store solutions, and appropriate there was a substantial amount of antioxidant activity soluble in 95 percent methanol to prepare 1 mM solution. After diluting with methanol, several cons. (2, 12, 32, and 95 M) of solutions was generated from the stock solutions. To the 2.5 mL of DPPH solution, 1 mL of chemical component was added. An Ultraviolet light spectrometer has been used to determine the absorption of component at 525 nm after 25 minutes. The absorb of a blank DPPH component without test substance was measured at 520 nm a control (A0), the below equation used to calculate the % of absorbance value.

Absorbance value = A_0-A_1/A_0 *100

Where.

A_0= DPPH absorb in absence of antioxidant

A_1= DPPH absorb in presence of antioxidant.

The compounds' IC50 values were also computed.

2.4.3 Anticancer properties

The ligand and M-compounds was tested in vitro against five distinct cancer cell types in humans, including MCF-7 a cell line for melanoma, HeLa cell line for carcinoma, A-549 carcinoma of the lungs cell line, and 293 renal cell line from a human fetus. The typical medication was cis-platin. The MTT-microcultured tetrazolium was use to identify cell ability in condition of evaluate substances. This is a colorimetric quantitative approach for identifying cell viability [35]. The metabolic activity of living cells is the metric being measured. After solubilization in DMSO, cells that are biologically active convert a light salt of yellow reagent was added (MTT) to water-insoluble bright blue precipitate this can be applied immediately measured. The quantity of live cells is directly proportional to the formazan absorbance. MCF-7, HeLa, A-549, and HEK293 on a 95-well plate, cells were concentration on a plate of 1 103 cells per excellent. A cell was cultivated in full medium overnight before being transferred to reduced serum media. As a control, 1 percent DMSO was employed. Following 45 hours of procedure with various doses of evaluated chemicals, the cells were cultured for a period of time in the CO2 chamber for 3 hours and MTT (3.0 mg/mL). The media was then withdrawn from each well, and 100 mL of DMSO was added to the precipitate was formed crystals must be dissolved. Optic density was determined by scanning the samples at 560 nm, connected using a cell amount, after thorough mixing. The percentage of viability was used to represent the results. All of the experiments were done three times. The IC50 graph pad prism was use to find the values. (5.05 version) using linear regression analysis, The IC50 value, which would be the amount needed, was used to compute the reaction factor to reduce cell viability by 50% [36].

2.5 Technique of calculation

2.5.1 Research on molecular docking

Research goal was to analysis the probable binding mechanisms with the aim EGFR protein complex body part by using models of docking studies and to explainer, interacting system of ligand and [Co(2-ANA)$_2$Cl$_2$], [Ni(2-ANA)$_2$Cl$_2$], and [Cu(2-ANA)$_2$Cl$_2$] complexes with target receptor. EGFR is a key player in cancer illness and a popular target for cancer inhibitors. Overexpression of EGFR is linked to a variety of malignancies, squamous-cell pulmonary cancer is one of the most common cancers (75 percent), of anal. tumors instances [37], glioblastoma (55 percent), and cancers of epithelium of both the neck and head (60 percent) (75-100 percent) [38]. The docking research was done with transition metals and ligands on the EGFR protein receptor. The RSC protein data library provided the EGFR crystal structures. The UCSF Chimera was use to purify the EGFR protein by eliminating water molecules and ligands. Chem Create Ultra 12.0 was use to draw the 3D geometry of M-complexes, and the 3D geometry

was thoroughly optimised[39-40]. In docking, motion-efficient proteins, ligands, and M-compounds was employed.

Molecular docking protocol

The stiff EGFR ligand and compounds developed created to bind with one another. in the ADT process. Interaction energies charges were created by combining non-polar H atoms, was apply to all partical of the protein structure. PDB geometry was translated to PDBQT form for future ADT research, and energy estimates were gone utilising strategies bases on genetics, non-polar H particle, Interaction energies fractional penalties, rotational bonds, and a carton matrix having sizes 60^3 A^o create around the EGFR specific protein was allotted by using Molecular docking instruments 1.5.6 and width of (Angstrom): 0.3750. The highest number of assessments and the population size were 160 and 21, 00,000, respectively. The results were investigated using Discovery Studio 4.1.0. The whole procedure explains how to dock EGFR inhibitors in detail, including the receptor–compound interactions' interaction efficiencies.

3. Analysis of the findings

All of the compounds are non-hygroscopic and very stable at normal condition. Table 1 shows that the metal complexes have a 1:2:2 stoichiometry (M: Ligan:Cl) based on analytical data. In DMF, CH_3OH, ethanol, and, DMSO, all of complexes are readily soluble.[41].

3.1 Spectral investigations in the infrared and Far-infrared

Table S1 shows the IR spectrum analysis of the ligands and M-compounds. The peak for N-H of NH2 of 2-ANA is 3386 cm^{-1}, a peak for C=O of CHO group is 1668 cm-1, and the peak for frequency of bending $\upsilon_{C=N}$ of (py) ring is 1585 cm^{-1}. The IR data of compounds was comparable to that of (2-ANA), with slight differences in peak positions. The $\upsilon_{C=N}$ (pyridine) peak was shift to a low wave number in all complex spectra when compared to the free ligand, showing that 2-ANA is coordinated through the pyridine ring nitrogen atom. The modern peaks at 465-420 cm^{-1} was attribute to M-N, whereas the peaks at 371, 312, and 285 cm^{-1} was allocated to $\upsilon_{MCl,}$ respectively [42-44].

3.2 UV-Vis spectra

The UV spectra of 2-ANA in DMF shows a wide band of absorbing at 265 nm, which has attribute to the pyridyl group's n→π*, and, π→π* transitions. The absorb peaks at 352 nm has attribute to an intra - molecular charge carrier zone formed by ligand's -NH_2 and -CHO subunits (2-ANA). Bands with distinct characteristics with minor changes in blue were also visible in the matching metal complexes. Because of the d7,d8, and d10 electronic configuration, no d→d transitions are predicted for Co(II), Ni(II), and Cu(II) compounds. Tetrahedral structure has postulated for M-compounds based on IR and analytical evidence.

3.3 NMR spectral studies

In (DMSO, ppm, 425 MHz), ^{1}H-nmr data of 2-ANA and compounds were recorded: The indications at δ 9.65 (s, ^{1}H), 8.83 (d, J = 9.14 Hz, ^{1}H), 8.35 (d, J = 9.18 Hz, 1H), 7.45 (s, 2H, -NH2), 7.79-7.91 (m, 1H). The ^{13}C-nmr data of 2-ANA shows signals from 113.14 to 193.25 ppm. Carbonyl compounds carbon has a signal near 192.75 ppm, tertiary carbon atoms have spikes between 152.65 and 112.85 ppm, and the other carbon atoms have spikes at 111.57, 143.28, and 155.45 ppm. These signals in complex data, which occurred, shifts caused by positive coordinating, suggest that 2-ANA's pyridine N is engaged in M-ion bonding.

3.4 Thermal gravimetric research

Figure S2 a-d shows the thermograms of ligand 2-ANA and their M-compounds. The Table S2 shows the stages of decomposition, temperature ranges, reported breakdown components and compounds, as well as the mass loose % estimate. All of the compounds were heated to temperatures ranging from 26 to775 degrees Celsius in a nitrogen environment. The ligand 2-ANA degraded in three steps, according to thermal data, from 52-225 ˚C, 212-465 ˚C and 465-712 ˚C for the loss of several pieces in order to keep C2 as a remnant, from 225-332 C, the Co(II) complex dissolved progressively, resulting in the loss of organic ligands, although CoCl2 was retained as a residue. Breakdown of the Co(II) complex began at 216-362°C for the disappearance of chemical compounds in order to keep CoCl2 residual, in contrast to decomposition of the Ni(ii) compound began at 173-451°C for continual weight reduces of ligands in order to use CoO as loss.

3.5 2-ANA and the [Co(2-ANA)2Cl2] compound crystalline structure

3.5.1 2-ANA

The ligand (2-ANA) crystallised in a mono-clinic arrangement a P21/c group of space and Z = 8. Table 2 lists the crystallographic parameters, whereas Table S3 lists the H-bonding data. An asymmetric unit in the crystal structure is made up of two 2-ANA molecules, designated a and b, that seem to have intra-molecular classic N-H.....O, where one of the amine group's H binds to an O atom in the aldehyde group in carbonyl compound, producing a 6-cyclic ring. Two different types of fundamental molecular motifs occur from inter - particle H-bonding among N-H.....N particles: N3-H3b.....N2 interactions in the inversion site of compounds in the multi-meric unit B and N_2-H_2b.....N_1 interactions A monomer is a single molecule A, which results in molecular stacking arrangement in the shape of a salmon bone the b axis. Furthermore, the pyridine ring's non-classical poor hydrogen bond couplings C-H...N units result in a unique dimeric unit pattern stacking .Figure S3 c. Furthermore, as shown in Fig. S4, the hydrogen aldehydic H_{12}, In inter-particle non-classical interactions, the pyridine circle proton H9 of dimmers CC* or H4 of molecules A interact. H-bonding to oxygen atom as tri-furcated receiver O1 in C-H.....O.The intermolecular weak H-bonding between molecule A's pyridine circle proton H3 with compound B's aryl atom of oxygen O2 extends the molecular stacking on a 2D structure (Fig. S5). Connections between the

reactive pyridine groups of dimeric units CC* that are caused by length. (length =3.89A^{o}) strengthen geometry of crystalline cohesiveness within the crystalline structure in atomic packing. In a word, 2-ANA's supra-molecular stacking shape is a 3D supra-molecular stack arrangement[44-45]. is made up of H-bonding can be classified as either classical or non-classical. networks, as seen in Fig. S6.

3.5.2 [Co(2-ANA)2Cl2] complex

In the triclinic system, the [Co(2-ANA)2Cl2] complex crystallised with the P-1 cluster of area and Z= 2. Table 2 lists the crystalloid graphic information. Table S3 shows the specifics of the H-bonding data. The atmosphere of cooperation surrounding the Zn atom is deformed tetrahedral shape, with two positions filled by 2-ANA's pyridine nitrogen atoms, A and B, and the other two sites held by Cl_1, Cl_2. Figure 2, depicts the ORTEP diagram of [Co(2-ANA)2Cl2], while Table 3 a list of the options inter-atomic distances and bond angles. H-bonding contacts, including classically and non-classical may be found in the Co(ii) compound, according to findings. The intra - molecular H-bonding N-H....O that can be seen in 2-ANA crystalline geometry is preserved in complex geometry. Furthermore, as illustrated in Fig. 2, the complex molecule contains intra-molecular H connections that aren't classical such as Cl..H-N occurring as N5-H5b•••Cl_2 and N3-H3•••Cl_1. Non-classical intermolecular hydrogen bonds are also present in the 2-ANA and [Co(2-ANA)2Cl2] complex, as they are in the free ligand. A few of the halide compounds participating in the C9-H9.....Cl2 hydrogen - bonding contact inside the inter-particle non-classical pyridine ring, resulting in 1-D the complex's sequence (Fig. S7). The bifurcated electrophilic atom of oxygen O1 of an aromatic rings of receptor A in compound particle acts as a twisted electrophile for pyridine ring hydrogens H3 and H4, whereas the H2 hydrogen and allyl hydrogen H5 of ligand A in same compound molecule take part in non-classical inter-molecular weak H-bonding with the bi-furcated electrophilic oxygen atom O2 of the binding site As a result, 2-ANA in the complexes is implicated in two kinds of inter-molecular bifurcation soft H-bonding with the aryl group's oxygen atom in 3D crystal structure. Figure S9, depicts the 3D network of non-classical H connections that exist.

3.6 Antibacterial properties:

The ligand 2-ANA has little action against the pathogens in vitro, but the complex [Co(2-ANA)2Cl2] has highly reactivity against S. aureus (13.7 g/mL) and medium reactivity versus three species: E. coli (30 g. mL^{-1}), K. pneumoniae (30 g. mL^{-1}), and B. subtilis (30 g. mL^{-1}). The compounds [Cu(2-ANA)2Cl2], [Ni(2-ANA)2Cl2] have influence to weak antibacterial properties versus, B. bacillus, S. aureus, K. pneumonia, and E. coli, in relation to reference compounds. Although 2-ANA has no action against the genus, the excellent activity shown by [Co(2-ANA)2Cl2] might be attributed to 2-ANA's coordination with Co (ii). The products' (MIC) are listed in Table 4. When comparison to [Ni(2-ANA)2Cl2] and [Cu(2-ANA)2Cl2] complexes, the [Co(2-ANA)2Cl2] combination had superior antibacterial activity. When compared to the [Cu(2-ANA)2Cl2] complex, [Co(2-ANA)2Cl2], and [Cu(2-ANA)2Cl2]

complexes have only modest activity against, E. coli, B. subtilis K. pneumoniae.

3.7 Anti - fungal properties:

The anti-fungal properties of 2-ANA and their M-compounds was tested in vitro versus by fungus strains A. niger and P. notatum, and results were comparison to reference medication Ketoconazole by using minimum inhibitory concentration (MIC) measurements. Table 5 shows that compound [Co(2-ANA)2Cl2] as very good anti-fungal properties versus P. notatum, A. niger, such values (12.4 g/mL, 12.4 g/mL), whereas the compound [Cu(2-ANA)2Cl2] as medium to low anti-fungal properties versus A. niger strains with values of 45 g/mL. Despite the fact that the ligand 2-ANA had no anti-fungal action, it did show good to moderate activity when bound to metal ions, which could be due to a synergistic effect. In comparison to other metal complexes, the Co (ii) compound as demonstrated very good action versus P. notatum, and A. niger.

3.8 Anti-oxidant properties

Table 6 shows the IC_{50} values of produce ligand as well as their coordination compounds; raising the conc. of the complex improves the exploring action. Figure 3 shows the percentage inhibition (IC50) of metal complexes (1-3). The findings shows that as comparison to transition metals, the scavenging ability of the free ligand (IC50 = 22.10±1.45 µM) is much lower. The [Co(2-ANA)2Cl2] compound has a high activity level, with an IC50 of 10.14±2.50 µM. With an IC50 of 14.20±2.69 µM, [Cu(2-ANA)2Cl2] exhibits considerable activity, whereas [Ni(2-ANA)2Cl2] exhibits medium nature versus an IC50 of 19.23±2.35 µM. The scavenging activity of the ligand and transition metals is rising in order based on their IC50 values.

2-ANA < [Ni(2-ANA)2Cl2] < [Cu(2-ANA)2Cl2] < [Co(2-ANA)2Cl2]

3.9 Anti-cancer properties

The anti-cancer properties of produce substances is test by using the MTT test with anti-cancer medication cis-platin as a reference versus, MCF-7, HeLa, HEK-293, and A549 cells. Curves of survival, A549, and MCF-7 were creating by plotting the association in between drug concentration as well as the survival percent. Table 7 shows the IC50 values for produce compounds versus cell lines that were examined. When compared to the conventional medication cis-platin, the [Co(2-ANA)2Cl2] complex showed considerable action versus 3 cancer lines MCF-7, HeLa, and A549, as well as IC50 values of 22.720.45 M, 18.070.28 M, and 18.280.24 M, respectively. With IC50 values of 23.170.31, 33.280.12, and 30.230.06 M, respectively, the [Cu(2-ANA)2Cl2] complex exhibits moderate activity, whereas the [Ni(2-ANA)2Cl2] complex exhibits limited activity with IC50 values of 41.540.27, 40.870.35, and 42.930.37 M, respectively. HeLa, MCF-7, and A549 cancer cell are all cytotoxic to the [Co(2-ANA)2Cl2]

complex. On studied cell lines, the [Ni(2-ANA)2Cl2] compound is not cytotoxic. Based on IC50 values, the [Cu(2-ANA)2Cl2] compound is solely cytotoxic to the HeLa cell line. On the HeLa cell line, the [Co(2-ANA)2Cl2] compound shows anticancer action. In conclusion, the [Co(2-ANA)2Cl2] complex has substantial activity, the [Cu(2-ANA)2Cl2] complex has moderate activity, and the [Ni(2-ANA)2Cl2] complex has limited activity versus MCF-7, HeLa, and A549.

4. Docking of molecules

The L and M-compounds have minimal coupling energies of -5.85, -6.69, -6.03, and -6.33 K cal/mol, approximately, for EGFR protein receptor. The peptide receptor was harmed by transition metal complexes more effectively than ligands, suggesting their ligands 2-ANA in compound have a tendency to horizon for creation of grille protein. In molecular docking, this entanglement forces experiments clearly suggest in anti-cancer properties findings, as shown, with metal compound having the loss hinge values and demonstrating good anticancer activity via interacting with the EGFR transporters for proteins, ligand and products attach to Hydrophobic connections and H-bonding connect with the EGFR specific protein, according to molecular docking studies. Instead of creating a cluster in the receptor's binding pocket, the drug 2-ANA forms a single molecule, Fig. 5 a-c shows optimum conformations of M-compounds such as $[Ni(2\text{-}ANA)_2Cl_2]$, $[Cu(2\text{-}ANA)_2Cl_2]$, and $[Co(2\text{-}ANA)_2Cl_2]$, Seven H bonds were found with the Ligand of M-compounds and EGFR protein receptor in the [Co(2-ANA)2Cl2]-receptor complex. Two H bonds, one interaction Lys721 and aldehyde group's O-atom, and other with N-atom of one 2-ANA's -NH2 group, had bond lengths of 2.17 A^0 and 1.62 A^0, respectively, and bond angles of 122.27 A^0 and 127.32 A^0 in complex. One H bond was discovered around Arg816 and O-particle of the aldehyde group, with a bond distance of 2.25 A^0 and a bond angle of 116.14 A^0 ; another H bond was discovered around Asn819 and H-particle of $–NH_2$ group, with a bond length of 2.34 A^0 and a bond angle of 117.67 A^0; and three leftover hydrogen bonds was form with Asp831. Bond distances of two H atoms from –NH2 set were engaged in bonding of 2.04 A^0 and 2.69 A^0, bond angles of 104.74 A^0 and 86.11A^0, respectively, some other H connection was created between H particle of –NH2 set of second 2-ANA of [Co(2-ANA)2Cl2] compound and bond length of 1.81A^0 and bond angle of 123.55 A^0. [Co(2-ANA)2Cl2] compound establishes repulsive contacts with amino acids Arg817, Asn818, Asp831, and Lys721 among these hydrogen bonding interactions.

When the ligand in [Ni(2-ANA)2Cl2]-receptor compound engaged effectively with protein receptor, two H bonds was generated. One H bond was establishes around Asp813 and H-atom of –NH2 group, with a bond distance of 2.36 A and a bond angle of 114.42, Another strong H connection was created in between two of them, Arg817 and N-particle of amine set, with a bond length of 2.13 A and a bond angle of 136.64.

Six hydrogen bonds were discovered in the [Cu(2-ANA)2Cl2]-receptor complex, In combination with Lys721 polypeptide chains, the N-particle of –NH2 and O-particle of the aromatic ring of 2-ANA receptor formed two H bonds surrounding them, bond lengths 2.13 A^0, 2.04 A^0 and bond angles 154.59, 112.87. Two bonds was form with ASP831 amino acids when they interacted with H atoms of 2-ANA's -NH2 group in compounds, and bond length of 2.31 A^0, 2.13A^0, and bond angles of 122.06, 97.88, and last two are Asn818 and Arg 817, both of which had an O-atom in the aromatic ring and a H atom, of 2-ANA's –NH2 group, with bond distances of 2.02 A^0, 2.29 A^0, and additional unfavorable contact with the amino acids, Thr830, Val702, Asn818, and Asp831 were discovered among these interactions. Only three hydrogen bonds were found in the ligand (2-ANA) protein complex. Two H bonds occurred around Cys751 and Hatoms of -NH2 group with bond lengths of 2.12 A^0 and bond angles of 95.86^0 and 101.1^0, respectively, Phe832 and O-particle of carbonyl set created one H bond with a bond length of 1.85 A0 and a binding energies of 148.26, by possessing seven hydrogen bonds[46-48], the [Co(2-ANA)2Cl2] complex has the lowest binding energy compared to [Ni(2-ANA)2Cl2] and [Cu(2-ANA)2Cl2]. The L and compounds with least binding energy exhibit strong cytotoxicity by using in anti-cancer tests. The results of docking research on molecules show they are highly correlated, given the anti-cancer data information from the experiments in vitro.

5. Conclusions

A number of spectroscopic methods were used to produce the ligand and M-compounds of Co(ii), Ni(ii), and Cu(ii), through N atom of pyridine ring, 2-ANA functions as a monodentate ligand towards metal ions, forming a tetrahedral shape surrounding the metal in the complexes. When compared to cis-platin reference drug, [Co(2-ANA)2Cl2] complex showed anti-oxidant properties with IC_{50} value of 12.142.50 M in IC50 values for DPPH radical scavenging experiment show significant anticancer effects versus HeLa, MCF-7, and A549 of 18.022.19 M, 20.711.32 M, and 16.260.26 M, respectively, in the MTT assay. This complex also show potent Anti-fungal properties versus A. niger and P. notatum species when comparison to Streptomycin conventional medication, and show anti-bacterial properties versus S. aureus microorganisms when comparison to Streptomycin conventional medication. Ketoconazole was use as reference drug. The [Co(2-ANA)2Cl2] compound has the least amount of binding energy of -6.89 K.cal/mol and had greater anti-cancer efficacy in molecular docking of molecular studies against the EGFR protein. The results of molecular docking are highly correlated with in vitro anticancer efficacy. In comparison to [Ni(2-ANA)2Cl2] and [Cu(2-ANA)2Cl2] compounds, [Co(2-ANA)2Cl2] compound was show to a powerful, , antibacterial agent, anticancer, and, antioxidant.

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