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Synthesis, Characterization and Molecular Docking studies of 4-amino Triazole derivative ligand and its Pb (II) complex.

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ABSTRACT: A triazole derived ligand, 4-amino-5-propyl-1,2,4-Triazole-3-thiol and its metal complex with Pb(II) ion was synthesized in solid state. The prepared compounds were characterized by elemental analysis and various spectral techniques like Infrared spectra, ^{1}H-NMR spectra, ^{13}C-NMR spectra. The FT-IR of Pb(II) complex indicates that binding is taking from amino N-atom and deprotonated thiol group. Molecular Docking studies revealed that prepared compounds have antibacterial potency.

KEYWORDS: Triazole, Metal complex, Synthesis, Spectra, Molecular Docking.

I. INTRODUCTION

Heterocyclic compounds find extensive use as pharmaceuticals, vetnary products, agrochemicals, corrosion inhibitors, copolymers and dyes [1]. Heterocyclics have shown great biological activity as antifungal, antibacterial, anti-inflammatory and herbicidal [2]. Triazoles belongs to heterocyclic compounds, their synthetic routes and biological activities have been studied extensively [3,4,5]. Metal based triazole derivatives have shown good biological activity due to chelation [6]. Amino-mercapto triazoles and their metal complexes have been synthesized and characterized by Tolan et al [7]. Cu(II) complexes with 3-substituted-4-amino-5-mercapto-1,2,4-triazole Schiff bases have been extensively studied by Moustafa et al [8]. Molecular Docking is a tool in computer-assisted drug designing which predicts the binding modes between a substrate and protein having known three dimensional structure [9]. The molecular docking of Ni(II) complexes of 3-pyridinyl-4-amino-5-mercapto-1,2,4-triazole have shown good inhibitory activity [10]. The present research work consist synthesis and characterization of 4-amino-5-propyl-1,2,4-triazole-3-thiol and its Pb(II) complex. The molecular docking study was performed against 1JIJ protein derived from Staphylococcus Aureus.

II. MATERIALS AND METHODS

Chemicals used in the experiment were AR/ACS grade. The melting point was determined by using capillary method using Kjeldahl flask. The elemental analysis data was taken using CHNS Analyzer : ELEMENTAR Vario EL III. The FT-IR spectra was recorded using FTIR spectrometer : Thermo Nicolet iS50 in the range 4000cm^{-1} – 400cm^{-1}. The ^{1}H and ^{13}C-NMR spectra was taken using CDCl3 solvent using 400 MHz FT NMR : Bruker Advance III. The molecular docking of the ligand and its Pb(II) complex was performed using CB-DOCK 2 server [11].

EXPERIMENTAL

1. Synthesis of Ligand, 4-amino-5-propyl-1,2,4-triazole-3-thiol [12]:

Equimolar amount of Thiocarbohydrazide and n-Butyric acid was fused at melting temperature for 15 minutes on oil bath. After cooling, 50ml water and 5ml conc. HCl was added. White coloured solid crystallizes, filtered, washed with 50% ethanol. The compound was recrystallised using ethanol. Colourless plates were obtained.

M.P - 107°C (Literature M.P - 106°C)

2. Synthesis of Pb(II) complex :

5mmol ligand and 2.5 mmol Lead(II) acetate.3H_2O was dissolved in methanol in separate beakers. Pb(II) acetate solution was dropwise added to ligand solution with constant stirring. White coloured metal complex separated, filtered, washed thoroughly with methanol and dried in dessicator.

III. RESULTS AND DISCUSSION

CHEMISTRY

The physico-chemical properties and Elemental analysis data are provided in Table-I and

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Table-II respectively. The ligand and its Pb(II) complex are non-hygroscopic in nature and stable in air. The ligand is soluble in common organic solvents but its Pb(II) complex is soluble in DMF and DMSO only. The metal complex decomposes at 172°C.

Table-I : Physico-Chemical properties.

Compounds	Colour	Solubility	Nature	Stability	Melting point
Ligand	Colourless	Methanol/Ethanol	Non-hygroscopic	Stable in air	107°C
Pb(II) complex	White	DMF/DMSO	Non-hygroscopic	Stable in air	172°C

Table-II : Elemental Analysis Data.

Compound	C%	H%	N%	S%	Metal%
	Found (Calculated)				
Ligand $C_5H_{10}N_4S_1$	37.96 (37.90)	06.37 (06.50)	35.41 (35.21)	20.26 (20.30)	-
Pb(II) complex $PbC_{10}H_{18}N_8S_2$	23.03 (23.10)	03.48 (03.70)	21.48 (21.50)	12.29 (12.49)	39.72 (39.50)

NMR Spectroscopy

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 0.992 – 1.029 (t, 3H, CH_3), 1.717 – 1.810 (m, 2H, CH_2), 2.716 – 2.754 (t, 2H, trz–CH_2), 4.659 (s, 2H, NH_2), 11.535 (s, 1H, SH).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) : 18.773, 24.890, 31.918, 158.530, 172.266.

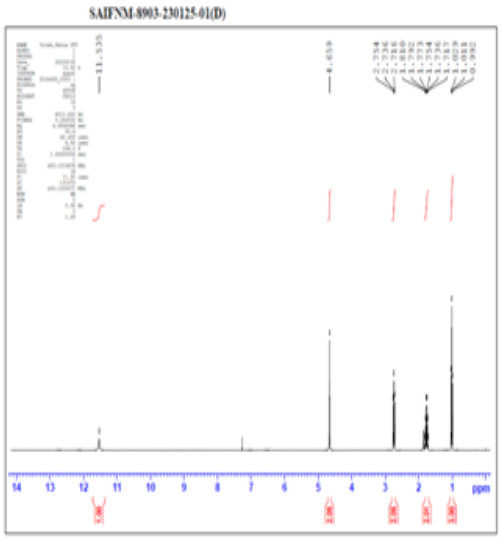

Fig. 1 : ^{1}H NMR spectra of Ligand

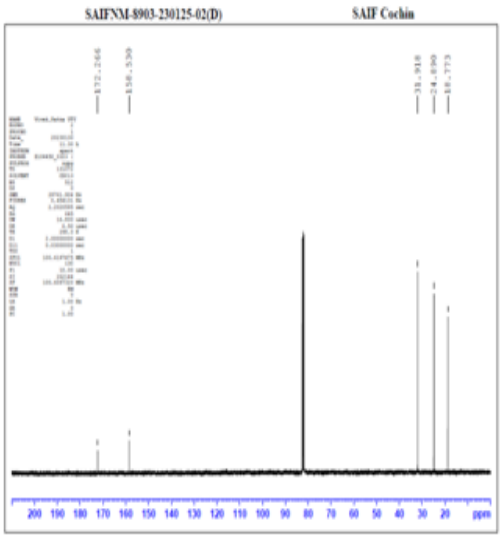

Fig. 2 : ^{13}C NMR spectra of Ligand

Infrared Spectra

The infrared absorption bands of ligand and Pb(II) complex and their corresponding assignment is provided in Table –III.

International Journal of Pharmaceutical Research and Applications
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Table-III : FT-IR spectral bands and assignments

IR frequency (cm^{-1})		Assignment
Ligand	Pb(II) complex	
3292.12	3174.81	Anti-sym. N – H stretch
3142.05	3037.73	Sym. N – H stretch
2966.16	2958.43	Anti-sym. C –H stretch
2941.60	2928.82	Sym. C –H stretch
2580	-	S –H stretch
1625	1638.64	C=N stretch(ring)
1599.70	1535.21	N –H bending
1501.46	-	Thioamide-I band
1472.48, 1388.82	1446.62, 1398.38	CH_2,CH_3 bending respectively
1324.20	1370.17	Thioamide-II band
1118.40, 1040.50	1063.02, 1033.82	NH_2 scissoring & rocking vib.
1000.31, 900.95	1001.53, -	Thioamide-III &Thioamide-IV
693.62, 671.01, 642.67, 591.03, 477.11	701.45, 688.40, 592.66, 471.25	Triazole ring deformation bands.

In the FT-IR spectra of the ligand, the peak at 3293.12 cm^{-1}, 3142 cm^{-1}, 2966.16 cm^{-1}, 2941.60 cm^{-1} are assigned to N –H anti-symmetric, N –H symmetric, C –H anti-symmetric and C –H symmetric stretch respectively. Thioamide bands have been also observed in spectra. A weak peak at 2580 cm^{-1} corresponds to S –H stretching. In the region below 700 cm^{-1} several triazole ring deformation peaks are observed.

The most fascinating feature of FT-IR spectrum of the Pb(II) complex is absence of S –H stretching band which is indicating that binding is taking place through deprotonated thiol group. The shift of N –H stretching band towards the lower frequency is revealing that amino N-atom is donating lone pairs to Pb (II) ion. From the data it is clear that ligand is bidentate and donating from S-atom and N-atom.

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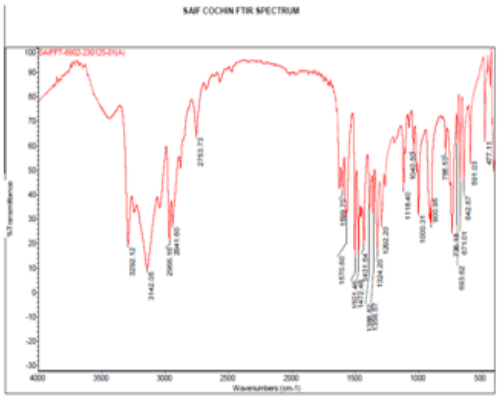

Fig.3 : FT-IR spectra of Ligand

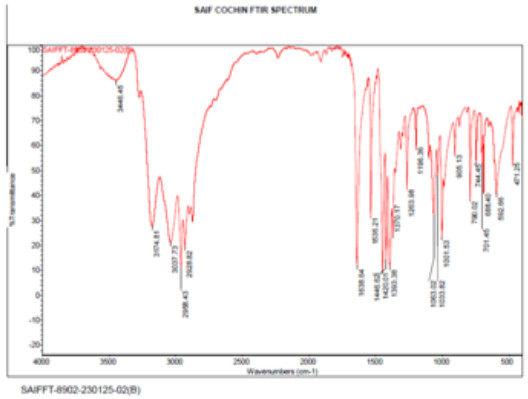

Fig.4 : FT-IR spectra of Pb(II) complex

Molecular Docking

The molecular docking between prepared ligand and target protein was performed using CB-Dock 2 server. Tyrosyl-tRNA Synthetase (1JIJ) derived from the bacteria Staphylococcus aureus was target protein. It plays an important role in protein synthesis of the bacteria and hence any compound which inhibits its action will be anti-bacterial in nature [13]. The docking scores and interactions are provided in the Table-IV. The prepared ligand shows a vina score of -5.2 which indicates that it will be antibacterial compound.

Compounds	Vina Score	Cavity Center ($A^{\circ 3}$)	Center (x,y,z)	Docking Size (x,y,z)	Amino acid residue contacts
Ligand (4-amino-5-propyl-1,2,4-triazole-3-thiol)	-5.2	2079	-14,18,83	17,26,26	TYR36 CYS37 GLY38 ALA39 ASP40 LEU70 THR75 ASP80 LYS84 ARG88 ASN124 TYR170 GLN174 ASP177 GLN190 ASP195 GLN196 ASN199

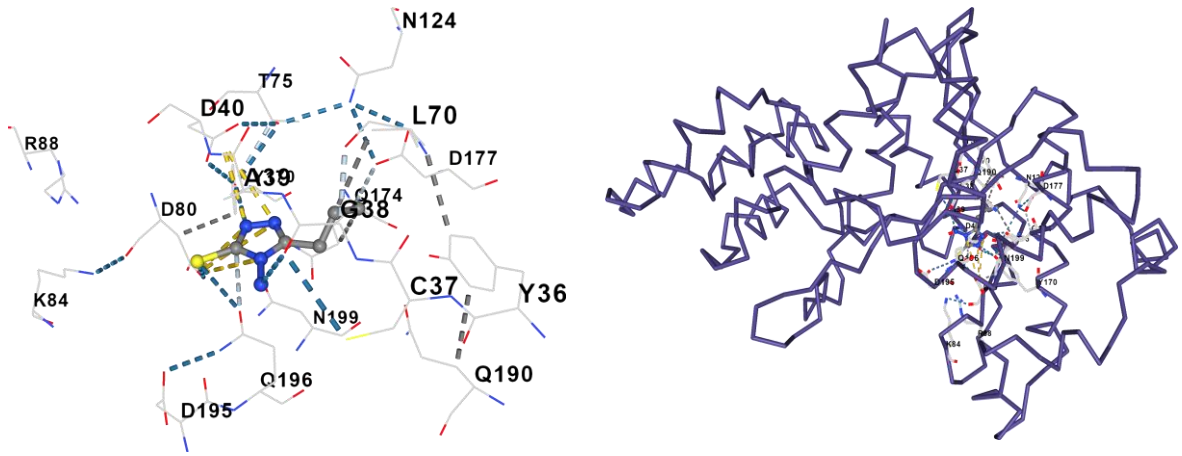

Fig. 5 : Interaction between 1JIJ protein and Ligand.

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IV. CONCLUSION

A triazole derived ligand, (4-amino-5-propyl-1,2,4-triazole-3-thiol) and its metal complex with Pb(II) ion was prepared in solid state. The synthesized compounds were characterized using micro-analytical and spectral techniques like FT-IR, ^{1}H NMR and ^{13}C NMR. The ligand is bidentate in nature and coordination in metal complex takes place through amino N-atom and deprotonated thiol S-atom. Pb(II) complex was tetrahedral in geometry. Molecular docking studies suggest that Ligand possess anti-bacterial property.

V. ACKNOWLEDGEMENTS

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