

Bio-Active Amino Acid Complex: Synthesis, Structure and Antimicrobial Activities

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ABSTRACT

A new Cu(II) complex with with amino acid and 4-Nitropyrazole have been prepared and structurally characterized by IR,LC-MS ,TG-DTA ,UV . Cu atom in the complex is coordinated by one oxygen and amine of Tyrosine ,de-protinated –NH of 4-Nitro pyrazole and three oxygens of aqua ligand forming octahedral based structure.Complex is screened for antibacterial and antifungal activity. In this review an over view on structure and anti-microbial activity of copper complex of amino acid and 4-Nitro pyrazole is presented.

KEY WORDS: Copper, Tyrosine, Anti-bacterial and anti-fungal activity.

1. INTRODUCTION

Coordination complexes are of great interest due to the special properties like electrical conductivity,sorption,catalysis and have their potential applications in biology. Due to the different oxidation states, transition metals can interact with a number of negatively charged molecules. Hence they have unique microbial activity which leads to the development of metal based drugs. A stable complex is formed by Cu(II)by chelating with amino acids.Amino acids are of great importance in biochemistry having both amine and carboxylic acid groups attaché to first carbon atom.They are known as α -amino acids ; out of 20 amino acids 9 are essential and others are essential in some ages or for medical conditions.Chemists have paid attention towards copper amino acid complexes because of its applications.According to previous investigations,reported structures of some copper complexes are given.

2. MATERIAL AND METHODS

IR spectra are obtained with a Shimadzu IR Prestige 21 FT-IR spectrophotometer. Electronic spectra are recorded on LABINDIA UV3000⁺ UV /VIS spectrophotometer. LC-MS spectra are recorded on AGILANT QQQ (ESI-MS). Mass spectrometer. TG-DSC spectra are obtained using SDT Q600 V20.9 BUILD 20.

Synthesis of [Cu(Tyr)(4NP)3(H₂O)]: An aqueous (5 ml) solution of Copper perchlorate (0.37g, 1.0 mmol) is added to an sodium hydroxide solution(10ml) of Tyrosine (0.181g, 1.0 mmol) under stirring conditions at 60°C, blue precipitate is formed and then aqueous solution(5 ml) of 4-Nitro pyrazole (0.113 g, 1.0 mmol) is added which turned to dark blue solution. After constant stirring at 60°C for 30 minutes. Blue precipitate is formed and washed with methanol. Yield is 0.35gm (52.1%). Anal. expt C₁₁H₂₇CuN₃O₈ ,Mol.Wt.,382.81 C, 34.51, H, 4.48, N, 10.98 (observed) C 34.20,H, 4.4, N, 10.58 (calculated). Important IR bands (KBR disc cm⁻¹) 3580, 3162, 1623, 1504, 1296, 759 cm⁻¹. Mass Peaks (m/z): 310, 391, 358, 413.

IR Spectrum of [Cu(Tyr)(4NP)3(H₂O)]: In the ligand spectrum the v(N-H) stretching vibration appeared at 3146 cm⁻¹ and is shifted to 3162 cm⁻¹ in the Cu(II) spectrum proving the involvement of the amino (NH₂) group in the complex formation. In free L-Tyrosine the band at 1600 cm⁻¹ is assigned to the anti-symmetric stretching vibration v_{as}(COO⁻) of L-Tyrosine. In the complex, this band is slightly shifted towards higher frequencies and appears at 1623 cm⁻¹. The spectrum range 1400- 1460 cm⁻¹ is characteristic of the symmetric stretching vibration v_{sym} (COO⁻). In this region in the L-Tyrosine spectrum, we found only one band of medium intensity at 1416 cm⁻¹, with a slightly marked shoulder at 1479 cm⁻¹, which is due to the symmetric carboxyl stretching mode v_{sym} (COO⁻). The v(OH) stretching vibrations do not emerge in the ligand spectrum, but they appear in the complexes spectrum at values between 3422 to 3580 cm⁻¹, suggesting the presence of the crystallisation water within these complexes. The NO₂ stretching frequencies for a N-nitro groups are found at lower wave numbers at 1296 cm⁻¹ for the symmetric stretching vibration and a higher wave numbers at 1623 cm⁻¹ for asymmetric vibration¹⁶⁻¹⁹. The bands at 1504, 1296 and 759 cm⁻¹ can be assigned due to the asymmetric and symmetric stretching and bending vibration of the NO₂ group respectively.important peaks reported in table.1

Table.1. IR Spectrum of [Cu(Tyr)(4NP)3(H₂O)]

Complex	v(N-H)	v _{as} (COO ⁻)	v _{sym} (COO ⁻)
	3146 cm ⁻¹	1600	1479 cm ⁻¹

LC-MS Spectrum of [Cu(Tyr)(4NP)3(H₂O)]:The Peak at 413(m/z) is assigned to Cu bound tyrosine, 4-nitro pyrazole and three water molecules [Cu(Tyr)(4-NP)3H₂O]. Peak at 391(m/z) and 358(m/z) correspond to removal of one water molecule [Cu(Tyr)(4-NP)2H₂O] and complete removal of water molecules from the complex [Cu(Tyr)(4-NP)]. The peak at 310(m/z) correspond to Cu bound to tyrosine and fragment of 4-Nitropyrazole.

Electronic Spectrum of [Cu(Tyr)(4NP)3(H₂O)]: The UV-VIS spectrum of the free ligands and their metal complex is recorded in DMF solution in the wavelength range 200–800 nm. The UV-Visible spectrum absorption bands of the complex showed bands in the ultraviolet region at 294 and 373 nm. It follows from the literature that the bands at 250-295 and 320 nm for Tyrosine and 4-NitroPyrazole, respectively, are related to the $\pi-\pi^*$ transitions of the pyridine, thiophene and benzene rings. The second absorption band in 4-NitroPyrazole at 373nm may corresponds to the n- π^* transition of the C= N group. The electronic spectrum of the Cu (II) complex 3 showed two ligand field bands at 294 and 373 nm. These bands are assigned due to d-d transitions respectively and denote an octahedral geometry. important peaks reported in table.2.

Table 2. Electronic Spectrum of [Cu(Tyr)(4NP)3(H₂O)]

	Absorbance	μ/cm^{-1}	Assignment
Complex	294	250-295	$\pi - \pi^*$
	373	320	n- π^*

TG-DTA spectrum of [Cu(Tyr)(4NP)3(H₂O)]: The thermal decomposition of the complex [Cu(Tyr)(4Np)3(H₂O)] is well defined and takes place in two stages. In the first step, loss of water molecules takes place in between 50-150° C with mass loss of 6.7% (obs 6.8%). This is indicated by DTA peak at 100°C, in the second stage which occurs in temperature range 250-300°C with DTA peak observed at 280°C this corresponds to the decomposition of Tyrosine, 4-NitroPyrazole. Observed mass loss is recorded as 84.3% (obs87.9%). The overall mass loss observed is 91% and it is compared with theoretical mass loss value which is found correct. The end product estimated is CuO. The observed mass and calculated mass are almost equal. TG-DTA graphs represented in fig.4 and 5

Proposed Structure of $[\text{Cu}(\text{Tyr})(\text{4-NP})_3(\text{H}_2\text{O})]$: In the title mononuclear complex $[\text{Cu}(\text{Tyr})(\text{4-NP})_3(\text{H}_2\text{O})]$ Cu(II) ion in the complex adopt perfect distorted octahedral based structure coordinated by one oxygen and amine of Tyrosine, one de protonated $-\text{NH}$ of 4-NitroPyrazole and three oxygens of aqua ligands.

Antimicrobial Screening of [Cu (Tyr)(4Np)3(H₂O)]: The complex is screened in vitro for Antibacterial activity against E.coli, S.aureus, P.aeruginosa and Antifungal activity against R.Oligospores by disc diffusion method. The Antimicrobial activity of the complex are listed in Table.3.

Table.3. Inhibition zone of Complex

Table 3: Inhibition zone of Compex	
Bacteria	Inhibition zone (mm)
E. coli	2
S.aureus	2
P.aeruginosa	3
Fungi	Inhibition zone (mm)
R.Oligospores	Nil

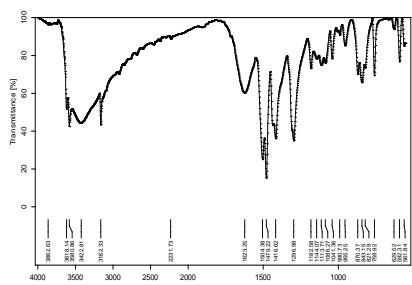


Figure 1. IR Spectrum of $[\text{Cu}(\text{Tyr})(\text{4Np})_3(\text{H}_2\text{O})]$

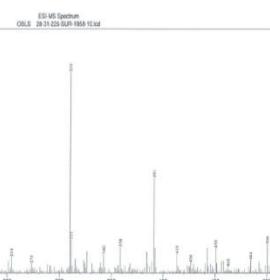


Figure 2. LC-MS Spectrum of $[\text{Cu}(\text{Tyr})(\text{4Np})_3(\text{H}_2\text{O})]$

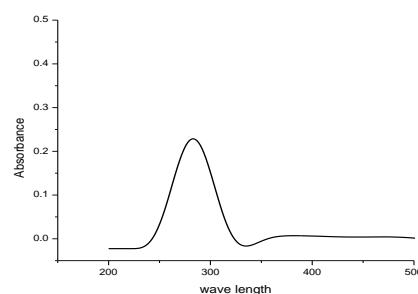
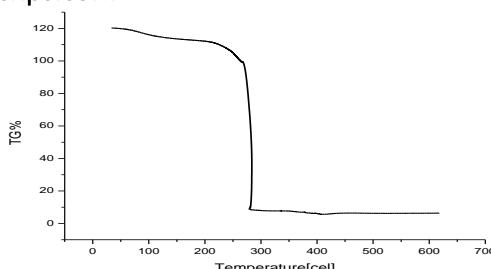
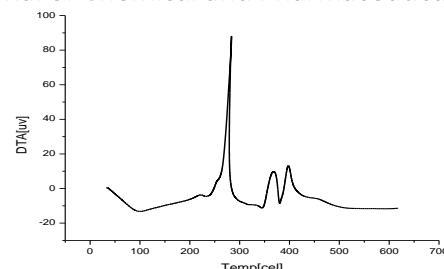
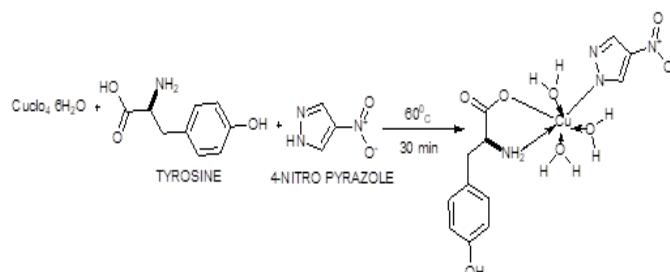


Figure 3. Electronic Spectrum of [Cu (Tyr)(4Np)3(H₂O)]

**Figure 4. TG Spectrum of [Cu (Tyr)(4Np)3(H₂O)]****Figure 5. DTA Spectrum of [Cu (Tyr)(4Np)3(H₂O)]****Figure 6. Synthetic route and proposed structure of complex****Figure 7. Inhibition zones for complex against *S.aureus*, *E.coli*****Figure 8. Inhibition zones for complex against *P.aeruginosa*****Figure 9. Inhibition zones for complex against *R.Oligospores***

3. RESULTS AND DISCUSSIONS

Transitional metal complex of copper involving amino acids like Tyrosine and 4-Nitropyrazole is synthesised by Self assembly method which were analyzed by means of IR,LC-MS ,UV and thermo-gravimetric method.

The IR spectrum showed that the Tyrosine act as bidentate ligand its coordination involving the carbonyl oxygen and nitrogen atom whereas 4-Nitropyrazole with N atom .The electronic spectrum confirms octahedral geometry for complex which is supported by LC-MS spectra.

The metal complex is screened for anti microbial activities are evaluated against three different bacteria (*E.coli*, *S. aureus*, *P.aeruginosa* and fungi *R.oligospores*) and the results demonstrated that complex exhibits good antibacterial activity in comparsion to standard drug like streptomycin.

Hence this new Bio-Amino acid complex which is endowed with potent anti microbial activity can be further used as drugs.

4. CONCLUSION

In this article we have reported the synthesis of copper,tyrosine, 4-NitroPyrazole and their antimicrobial studies. The results for complex revealed that they are good in microbial activity.

REFERENCES

- Apfelbaum-Tibika F, Bino A, Complexes of Dimolybdenum(II) with DL-Amino Acids, Inorg. Chem, 23, 1984, 2902-2905.
- Dondoni A, Massi A, Minghini E, Bertolasi V, Multicomponent Hantzsch cyclocondensation as a route to highly functionalized 2- and 4-dihydropyridylalanines, 2- and 4-pyridylalanines, and their N-oxides, preparation via a polymer-assisted solution-phase approach, Tetrahedron, 60, 2004, 2311-2326.
- Iqbal M.Z, Khurshid S, Iqbal M.S, Antibacterial activity of copper-amino acid complexes, J. Pak. Med. Assoc., 40 (9), 1990, 221.

Janssen J.W.A.M, Habraken C.L, Pyrazoles VIII Rearrangement of N-nitropyrazolesFormation of 3-nitropyrazoles, J. Org. Chem., 21, 1971, 3081–3084.

Janssen J.W.A.M, Koeners H.J, Kruse C.G, Habraken Pyrazoles XII Preparation of 3(5)-nitropyrazoles by thermal rearrangement of N-nitropyrazoles, J. Org. Chem., 38, 1973, 1777-1782.

Ohata N, Masuda H, Yamauchi O, Programmed Self-Assembly of Copper(II)-L- and -D-Arginine Complexes with Aromatic Dicarboxylates to Form Chiral Double-Helical Structures, Angew. Chem. Int. Ed. Eng., 35, 1996, 531.

Refat MS, El-Korashy SA, Ahmed AS, Preparation, structural characterization and biological evaluation of L-tyrosinate metal ion complexes, A.S. Journal of molecular structure, 881, 2008, 28-45.

Wang R, Zheng Z, Jin T, Staples R.J, Coordination chemistry of lanthanides at high pH, Synthesis and structure of the pentadecanuclear complex of europium(III) with tyrosine, Angew. Chem., Int. Ed, 38, 1999, 1813-1815.

Wojciechowska, Agnieszka & Daszkiewicz, Marek & Bieńko, Alina. Polymeric Zn(II) and Cu(II) complexes with exobidentate bridging L-tyrosine, Synthesis, structural and spectroscopic properties, Polyhedron, 28, 2009, 1481-1489.

Yamauchi O, Odani A, Takani M. Metal-amino acid chemistry weak interactions and related function of side chain groups, J. Chem. Soc. Dalton. Trans., 2002, 3411.