GROWTH, CHARACTERISATION, NLO AND DOCKING STUDIES OF ZINC COMPLEX OF (2R, 3R)-2-AZANIUMYL-3-HYDROXYBUTANOATE

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Abstract

Single crystals of Zinc complex of (2R, 3R)-2-Azaniumyl-3-Hydroxy Butanoate (Zn-AA) was synthesized by controlled slow evaporation method at 5°C. Zn-AA was dissolved in 50 ml of ethanol taken as the solvent. Single crystals of Zn-AA obtained after 15 days were washed, dried and characterized using FT-IR, UV-VIS spectroscopic studies, TGA-DTA and PXRD studies. Zn-AA is then subjected to NLO studies and Docking studies with two deadly COVID strains, COVID-7N0R and COVID-7R98.It is found that the complex Zn-AA is two times more effective in binding with COVID-7N0R than with COVID-7R98.It also shows excellent NLO properties.

Keywords: Azaniumyl-3-hydroxybutanoate, slow evaporation, NLO property, Docking, COVID strains.

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1. Introduction

Molecular level interactions involving carbon and non-carbon entities results in the emergence of novel molecules with diverse applications. Metal ions play a vital role in the mediation of reactions of carbon compounds. Aliphatic alpha aminoacids are the key molecules that involve in the formation of proteins, the building blocks of all living matter. Understanding the chemistry behind the interaction between metal ions and aminoacids can unearth facts regarding the formation of new complexes, that can be used in various fields ranging from drugs to dyes.[1,2]This study involves the growth of L-Threonine Zinc complex single crystals by slow evaporation method. The grown crystals were characterised by UV-VIS, FT-IR, PXRD and TGA-DTA studies. The grown crystals NLO applications were studied. Its use as a potential drug were also studied through molecular docking with two covid strains COVID-7N0R and COVID-7R98.

2. Materials and Methods

Single crystals of Zinc complex of (2R,3R)-2-Azaniumyl-3- hydroxy butanoate (Zn-AA) was synthesized by controlled slow evaporation method at 5°C[3].The ligand AA and the metal salt $ZnSO_4$ were taken in the ratio 3:1 and dissolved in 1:1 ethanol-water mixture. All chemicals used were of AR grade, obtained from Qualigens India. A grade glassware and deionised water were used for the preparation and growth of the Zn-AA crystal. The dissolved mixture of the ligand and the metal salt was refrigerated at 5°C for 15 days. Colourless transparent single crystals of Zn-AA were obtained. It was gently washed with the same solvent, dried and subjected to characterisation studies.

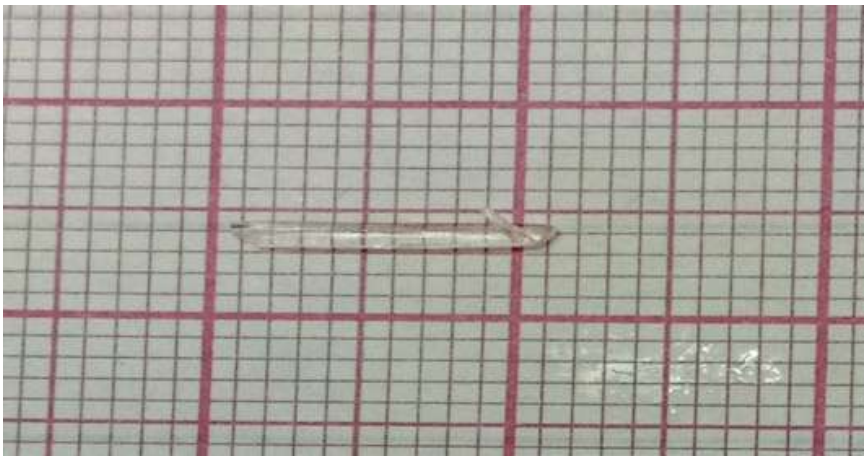


Fig-1-Single crystal of ZnAA complex

3. Results and Discussion

FT-IR STUDIES OF Zn-AA Complex

A broad and strong band in the 3187 cm-1 region is accounted for the H-bonded amine group with neighbouring carboxylic acid oxygen – N-H----O--. The carbonyl band is obtained at 1622cm^{-1} and C-O stretching band was observed at 1397 cm^{-1}. M-O band is observed at 614 cm^{-1} and M-N band is obtained at 774 cm^{-1}[4]. Based on the IR data of the complex, the ligand AA is bidentate in nature, binding with the metal ion through carboxylate oxygen and amine group.

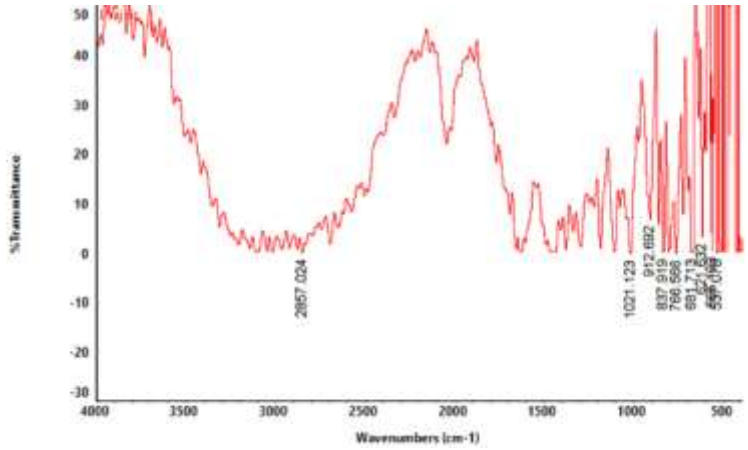


Fig-2 FT-IR of AA ligand

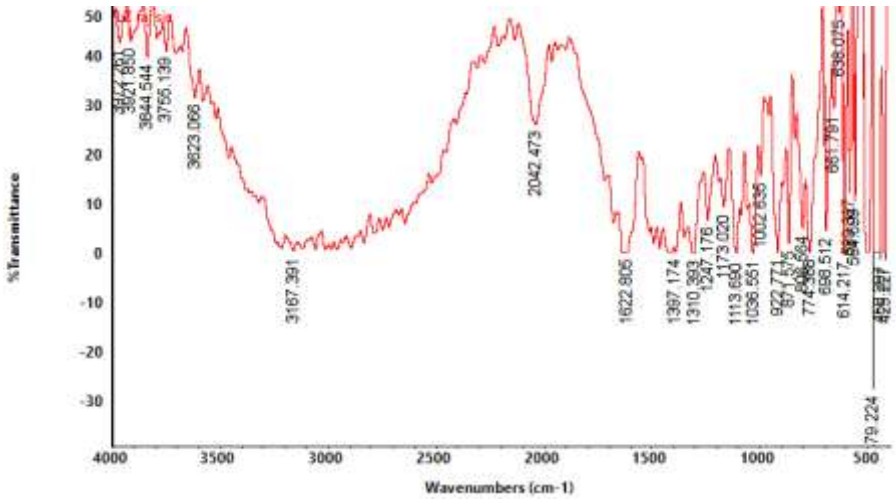


Fig-3 FT-IR of Zn-AA Complex

UV-VIS studies of Zn-AA

The UV-VIS absorption at 250 nm is due to the π-π* transition of the carboxylate group. As the d orbitals are completely filled in Zinc, no d-d transition is observed [5]. UV-VIS absorption seen only in the UV region is due to the fact that the complex is colourless. The UV-VIS spectrum of the complex Zn-AA is shown in Fig -4

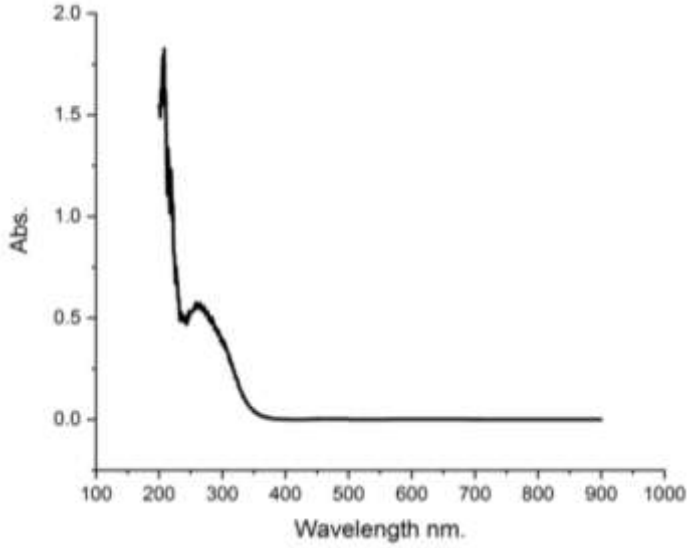


Fig-4 UV-VIS of Zn-AA complex

Thermal Analysis of Zn-AA complex

Thermal Analysis of Zn-AA complex were recorded in an inert atmosphere of Nitrogen. The complex is thermally stable upto 278 °C as shown by a strong endothermic peak. After that 95% of the mass is decomposed and a small residue of the metal oxide is left behind[6]. This is evident from the exothermic peak at 500°C.This shows that AA is organic in nature and is decomposed at low temperatures.

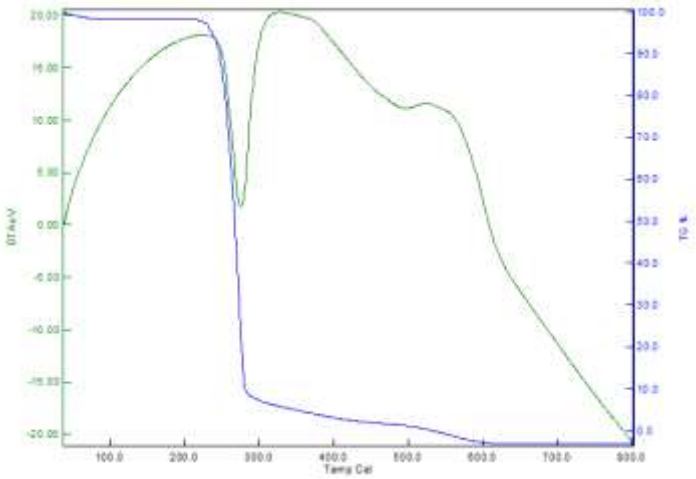


Fig- 5 Thermal analysis of Zn-AA complex

Powder XRD studies of ZnAA complex

Fig-6 shows the powder XRD pattern of the complex. All the scatterings are observed at low angles and are well defined. This indicates that the complex is a crystalline solid with porosity [7]. The metal ion may be incorporated in the interplanar space in the ligand **AA** and to form the complex [8]. The complex Zn-AA may have octahedral geometry with metal as its centre [9].

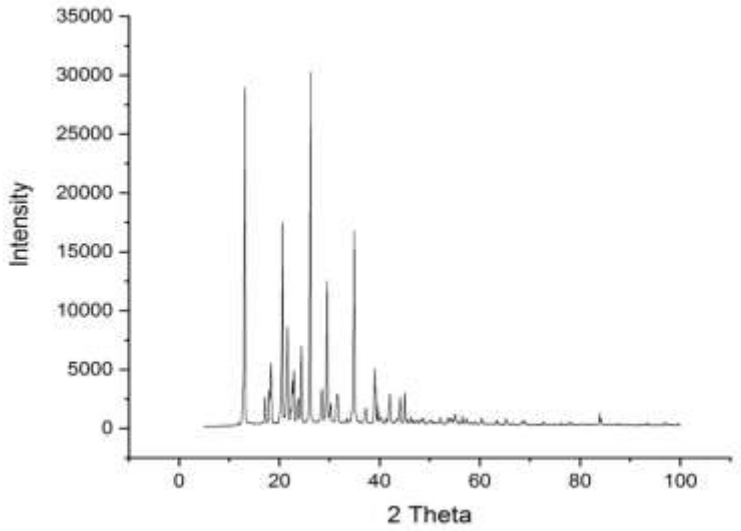


Fig-6 PXRD patterns of Zn-AA complex.

Structure of Zn-Aa Complex

The computational structural parameters of Zn-AA is given in Table-1

Atom pair	Bond length A° ZnAA
O1-O2	2.2467
O1-N3	2.8745
O1-C4	1.2029
N3-O5	2.5427
O5-C6	2.4593
C6-H7	1.0936
C6-H8	1.0918
C6-H9	1.0942
O5-C10	1.4289
C10-H11	1.1043
N3-C12	1.5338
C12-H13	1.0921
N3-H14	1.0218
N3-M15	1.8029
N3-H16	1.0329
O5-H17	0.9670

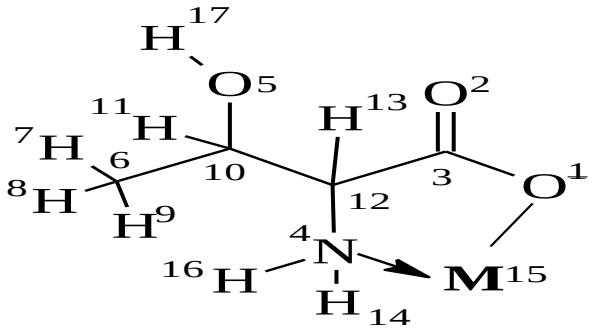


Fig-7.1 2D structure and numbering pattern of Zn-AA complex

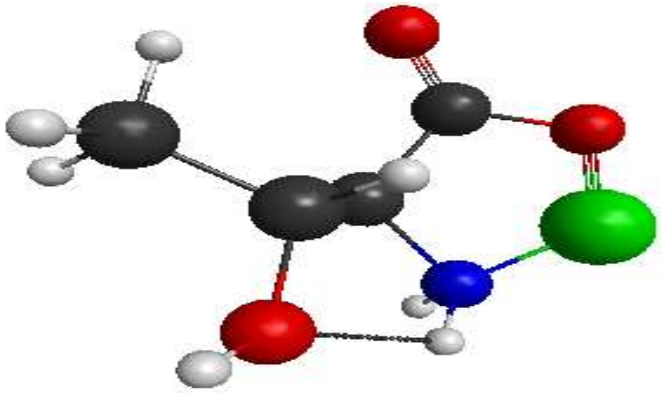


Fig-7.2 3D structure of Zn-AA complex (M-green; O-red; C-black; H-white ; N-blue)

Here the ligand AA is bidentate, as it forms a bond with the metal ion through the carboxylate group and a co-ordinate bond through the amine nitrogen. The total charge on the Zn-AA complex is +1. There is a slight elongation in the C-O and C-N bond lengths due to their involvement in the complex formation process[10].The order of N3-M15 and O1-M15 bond length is equivalent to the order of covalency of the complex. The bond angle O1-M15-N3 indicates that the complex has an octahedral geometry. The dihedral angle values show that the complex is non-planar.

Atom pair	**Bond angle (°)**
	ZnAA
O1-O2-N3	90.5875
O1-O2-C4	30.0841
O1-N3-O5	108.6219
N3-O5-C6	100.2986
O5-C6-H7	89.7345
C6-H7-H8	108.8508
C6-H7-H9	108.1158
N3-O5-C10	71.4231
O5-C10-H11	109.487
O1-N3-C12	60.0564
N3-C12-H13	107.8271
N3-C12-H14	110.3098

N3-H14-M15	41.241
N3-H14-H16	106.926
O5-C10-H17	110.0704

Atom pair	**Bond order ZnAA**	**Atom pair**	**Bond order ZnAA**
1-2	0.071	1-4	1.036
2-4	1.867	3-12	0.785
3-15	0.589	3-16	0.78
5-10	0.889	5-16	0.088
6-7	0.949	6-8	0.928
6-10	1.009	10-11	0.921
12-13	0.915		

Atom pair	**Bond order ZnAA**
1-15	0.786
3-14	0.846
4-12	0.889
5-17	0.85
6-9	0.947
10-12	0.947

Non-Linear Optical Properties of Zn-AA Complex

	Axis	**Polarisability(au)ZnAA**
Dipole	z	1.0319
Alpha	xz	-9.6040
Alpha	yz	3.3437
Alpha	zz	73.2091
Beta	xzz	-245.3349
Beta	yzz	46.7662
Beta	zzz	187.8563
Gama	zzzz	21697.9030

The NLO studies of the prepared complex Zn-AA shows that polarisation of the complex is higher than that of the ligand AA. This implies that metal ion Zinc, increases polarisation through the formation of the complex with the ligand[11].The order of polarisability is gamma > beta > alpha and higher along the – z- direction. The NLO properties of Zn-AA is given in Table-5

Atom pair	**Dihedral angle (°) ZnAA**
O1-O2-N3-C4	8.2169
O1-O2-O5	-59.0913
O1-N3-O5-C6	37.6462
O2-O5-C6-H7	101.8472
O2- C6-H7-H8	45.1813
C6-H7-H8-H9	-117.8585

O1-N3-O5-C10	17.936
O5-C6-C10-H11	122.5002
O1-N3-C4-C12	-14.2171
N3-C10-C12-H13	119.6278
N3- C12-H13-H14	22.0124
N3- C12-H14-M15	178.1182
N3- H14-M15-H16	41.2192
O5-C10-H11-H17	69.7213

Molecular Docking Studies of Zn-Aa

Docking of ZnAA with COVID-7R98			
Mode	**Binding energy (kcal/mole)**	**Cluster r_{msd}**	**Reference r_{msd}**
1	-6.88	0.00	37.52
2	-6.26	0.00	44.22
3	-5.97	1.54	44.00
4	-5.91	1.48	43.75
5	-5.89	1.46	43.90
6	-5.87	1.59	43.76
7	-5.85	1.41	44.62
8	-5.83	1.55	43.47
9	-5.83	1.46	43.66
10	-5.82	1.43	44.67

Hydrogen bonds

Index	**Residue**	**AA**	**Distance H-A**	**Distance D-A**	**Donor Angle**	**Protein donor**	**Side chain**	**Donor Atom**	**Acceptor Atom**
1	161B	LEU	2.13	2.66	112.83	no	no	6996 [O3]	2163 [O2]
2	161B	LEU	2.22	3.07	168.91	yes	no	2160 [Nam]	6992 [O2]
3	163B	GLN	2.31	3.29	158.71	no	yes	6989 [N3]	2183 [O2]

Metal complexes

Index	**Residue**	**AA**	**Metal**	**Target**	**Distance**	**Location**
Complex 1: Zn, trigonal.pyramidal (3)						
1	1A	UNL	6993	6986	1.80	ligand
2	1A	UNL	6993	6986	1.80	protein.mainchain
3	1A	UNL	6993	6996	2.97	protein.mainchain

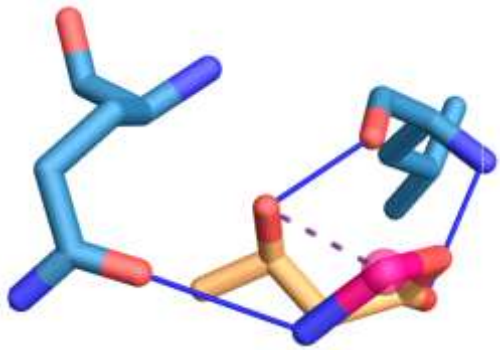
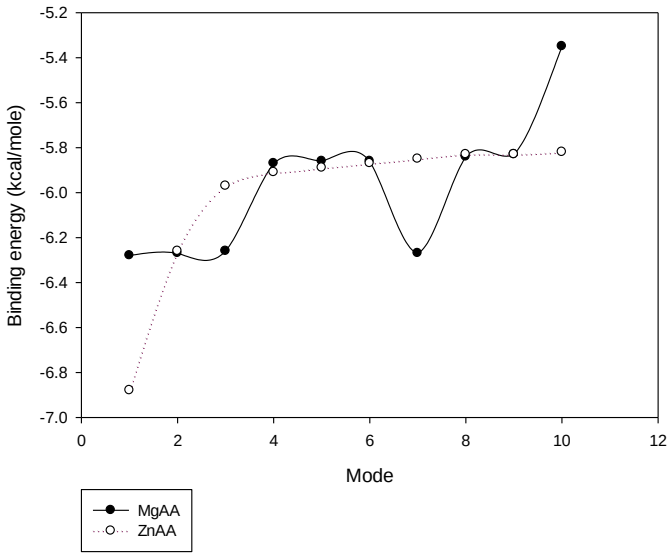


Fig- 8 ZnAA with COVID-7R98

BINDING ENERGY



Docking of ZnAA with COVID-7N0R			
Mode	**Binding energy (kcal/mole)**	**Cluster r_{msd}**	**Reference r_{msd}**
1	-6.40	0.00	28.35
2	-6.22	0.00	15.45
3	-5.70	1.66	15.05
4	-6.09	0.00	23.00
5	-5.82	1.46	23.20
6	-5.76	1.57	22.90
7	-5.86	0.00	12.80
8	-5.69	0.00	28.67
9	-5.66	0.20	28.75
10	-5.66	0.00	27.68

Hydrogen bonds									
Index	**Residue**	**AA**	**Distance H-A**	**Distance D-A**	**Donor Angle**	**Protein donor?**	**Side chain**	**Donor Atom**	**Acceptor Atom**
1	105A	SER	2.07	2.89	165.20	yes	yes	576 [O3]	4806 [O2]
2	173B	ALA	2.14	2.75	127.81	yes	no	2445 [Nam]	4810 [O3]
3	173B	ALA	2.25	2.65	103.63	no	no	4810 [O3]	2448 [O3]
4	174B	GLU	1.94	2.65	124.25	no	yes	4803 [N3]	2458 [O2]

Salt bridges						
Index	**Residue**	**AA**	**Distance**	**Protein positive**	**Ligand Group**	**Ligand Atoms**
1	59A	HIS	4.36	yes	Carboxylate	4800, 4806

Metal complexes						
Index	**Residue**	**AA**	**Metal**	**Target**	**Distance**	**Location**
Complex 1: Zn, square.planar (4)						
1	1A	UNL	4807	4800	1.80	ligand
2	1A	UNL	4807	4800	1.80	protein.mainchain
3	1A	UNL	4807	4810	2.99	protein.mainchain
4	173B	ALA	4807	2448	2.39	protein.mainchain

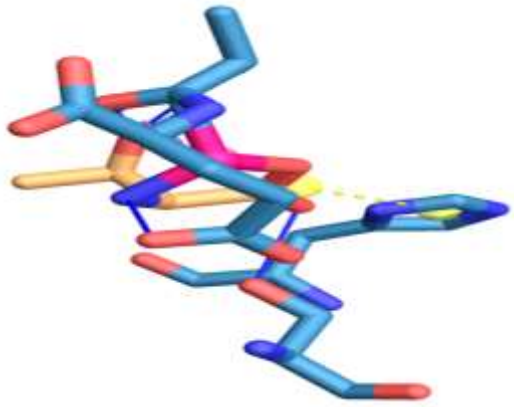
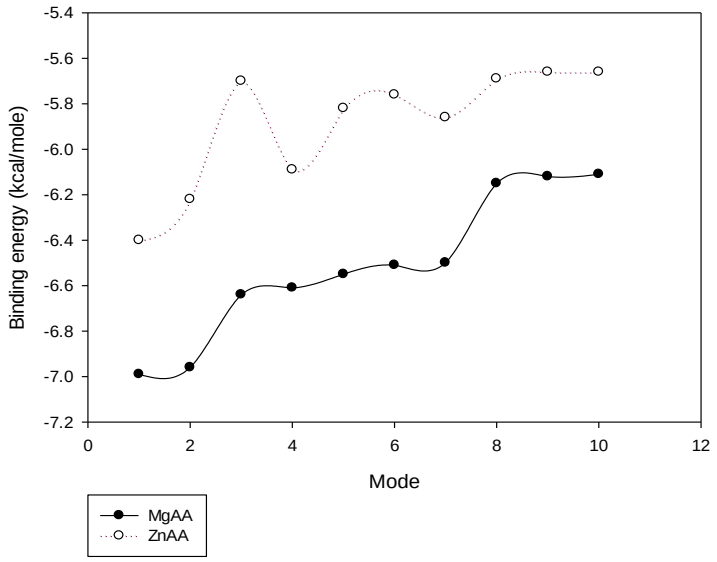


Fig- 8. 2 ZnAA with COVID-7N0R

BINDING ENERGY



The docking effect of the complex ZnAA is higher than that of the ligand AA.The docking effect of the complex is higher with COVID -7N0R than with COVID-7R98 by 8.4 %.The Zinc complex- COVID 7N0R protein interactions are through hydrogen bond formation with glutamic acid, salt bridge with histamine and complex formation with protein.The Zinc complex-COVID 7R98 protein interactions are through hydrogen bond formation with glutamine and complex formation with protein.

4. Conclusions

The single crystal Zn-AA is a colourless and transparent solid. Based on the FT-IR studies, the ligand AA is bidendate, binding the metal ion through carboxylate oxygen and amine group. It also confirms the presence of the functional groups present in the complex. The UV-VIS shows absorption at 250 nm due to the π-π^* transition involving the carboxylate group. The ligand AA is removed at 500°C showing that AA is organic in nature and decomposes at low temperature. The presence of the zinc metal ion stabilizes the ligand. Bond angle measurements show that the complex ZnAA is octahedral and dihedral angle shows that the complex is non-planar. NLO studies show that the ZnAA complex has higher polarisation than the ligand. This is due to the complex formation through its electron donating and accepting groups. Molecular docking studies show that the ZnAA complex binds through hydrogen bond formation,hydrophobic interaction,π stacking and complex formation with the proteins. The complex docks more effectively with COVID7N0R than with COVID7R98.This proves that the metal complex can act as an effective drug carrier.

5. References

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