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SPECTROSCOPIC AND ANTIMICROBIAL STUDIES OF SOME NOVEL COMPLEXES OF d^{10} METAL IONS.

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ABSTRACT: Complexes of kynurenic acid (KYNA) with d^{10} metals have been synthesized and their physicochemical peoperties were investigated using elemental analysis, IR, molar conductance, uv- visible and mass spectroscopy. Kynurenic acid acts as a chelating agent coordinating through the oxygen and nitrogen atoms of >O-H ,>C=N groups, respectively. Thermal stability and mechanism of decomposition of complexes were determined by TGA – DSC techniques. The ligands and its complexes were screened for their antibacterial activities towards Bacillus, Salmonellatyhi A, Escherichia coli and Staphylococcus aureus.

Key words: Kynurenic acid, d^{10} metal complexes, Antibacterial activity.

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INTRODUCTION

The inter disciplinary area of coordination chemistry is very important.. There are a number of applications of chelate compounds in laboratory, medicinal chemistry, electronics, catalysis etc. Kynurenic acid (KYNA) (IUPAC name 4-oxo-1H-quinoline-2-carboxylic acid), a major tryptophan metabolite, is a glutamate receptor antagonist, which is also reported to inhibit nicotinic acetylcholine receptors. The co administration of endomorphin-1 (EM1) with KYNA causes an enhanced antinociceptive effect.

KYNA levels are elevated in the brain and cerebrospinal fluid of persons with schizophrenia and Alzheimer's disease, both of which are characterized by deficits in contextual learning and memory. That elevated concentration of endogenous KYNA interferes with contextual learning and memory and support the notion that increased concentration of KYNA may contribute to cognitive dysfunction. In addition, data provides new insight into how novel 'gliotransmitters' may modulate neuronal function and behaviour (Chess, et.al., 2009).

EXPERIMENTAL

The complexes were made between the ligand and d^{10} metals, according to the standard procedure (Haresh, et.al., 2015). 0.2M solution of perchloric acid was prepared .The exact strength was determined by $_{P}$H metric-titration. Metal perchlorate solution was prepared from metal carbonate and perchloric acid. 25ml 0.2M metal perchlorate solution and 25ml 0.2M KYNA solution which is made in DMSO were mixed and refluxed for 2.5 to 3 hours at 90°C temperature and then cooled. This resulted in the solid product. The complex thus obtained was washed well with warm water and alcohol for the removal of unreacted metal salt and ligand. All the complexes were dried in oven at 40°C to 45°C temperature. In this way, the complexes of Zn(II), Cd(II), and Hg(II) were prepared and isolated as solid. An antibacterial study was carried using Agar Diffusion Method.

RESULTS AND DISCUSSIONS

Results of Infrared Spectra

KYNA and metal KYNA complexes were characterized by infrared spectroscopy. IR Spectra of the KYNA and the complexes were recorded on an FTIR instrument in the range 500-4000cm^{-1}. KYNA contains the functional groups, carboxyl, hydroxyl, amine, and a benzene ring, which are detectable by infrared spectroscopy (www.hindawi.com). Some of frequencies were changed and some of them eliminated. In KYNA the signal at 3434 cm^{-1} was derived from the stretching vibration of –O-H phenolic group. Stretching vibration of –O-H phenolic group for the complexes of Zn, Cd, and Hg in sequence are 3193, 3200, 3199 cm^{-1}. These values show that the –OH phenolic group is not coordinated to the metal ions. In KYNA carboxyl group stretching vibration of –O-H gives signal at 3105 cm^{-1} (acidic –OH). In metal complexes the acidic –OH frequency disappears. In KYNA the small signal at 2967 cm^{-1} is associated with the C-H bond of the quinoline ring (Ar-CH- streching) while in the complexes this absorption band gets higher in sequence for Zn, Cd and Hg, it appeared at 3105, 3085 and 3086cm^{-1}. The signal at 1593 cm^{-1} corresponds to the double bond C=N in quinoline ring, in complexes it appears at 1435, 1446 and 1446cm^{-1} for Zn-KYNA, Cd-KYNA and Hg-KYNA respectively. Some new frequencies appear in metal complexes in the favour of M-N and M-O, for Zn-KYNA it shows at 516, 635, 665 cm^{-1}, for Cd-KYNA 520,635,664cm^{-1}, for Hg-KYNA 520,636,664 cm^{-1}. Since the symmetric stretching vibration at 3105 cm^{-1} (acidic –OH) are not seen in the spectra of complexes, it is confirmed that the oxygen atoms of carboxyl group are creating complexes with metals which are bound with nitrogen of the quinoline ring. In KYNA at 1380 cm^{-1} wagging and twisting vibrations are present. CH_2 scissoring and asymmetric vibrations appear in Cd-KYNA and Hg-KYNA at 1446 cm^{-1} and in Zn-KYNA it appears at 1435 cm^{-1}.

TLC (solvent toluene: methanol 7:3) and M.P. was taken by melting point apparatus. Metal Complex formation was confirmed from TLC single spot reading. The UV – visible spectra were measured on a UV-1800 Shimadzu (Double beam) spectrophotometer.

Table 1: Results of Physical Measurements

Complex	Colour	M.W. (gm/mol)	M.P.˚C	Uv-vis spectral λmax (nm)	R.F. value*	Molar Conductance (℧) mho cm^{-1}	% yield
Ligand (KYNA)	Light cream	189.17	269	346.50 291.50 258.00	0.8503	2.55×10^{-3}	----------
Zn-KYNA	Cream	479.74	270	360.00 345.50 291.50 247.50	0.7368	1.38×10^{-3}	22.09
Cd-KYNA	Cream	769.92	268	361.00 345.50 289.50 236.00 213.50	0.8857	3.97×10^{-3}	19.099
Hg-KYNA	Cream	768.1	269	361.00 345.00 291.50 245.50	0.8346	3.53×10^{-3}	12.01

* Solvent system: (Toluene: methanol 7:3)

Table 2: CHN and Metal Analysis

Elemental analyses were performed with a Vario-MICRO CUBE C, H, N analyzer.

Metal Complexes	C (%)		H (%)		N (%)		Metal (%) by TGA	
	Found	Calculated	Found	Calculated	Found	Calculated	Found	Calculated
Zn-KYNA	59.82	50.02	4.249	2.91	6.92	5.83	3.443	13.63
Cd-KYNA	57.15	46.75	4.407	2.72	6.25	5.45	2.0	14.60
Hg-KYNA	62.54	46.86	3.90	2.73	7.27	5.46	2.03	26.11

TGA- DSC Analysis

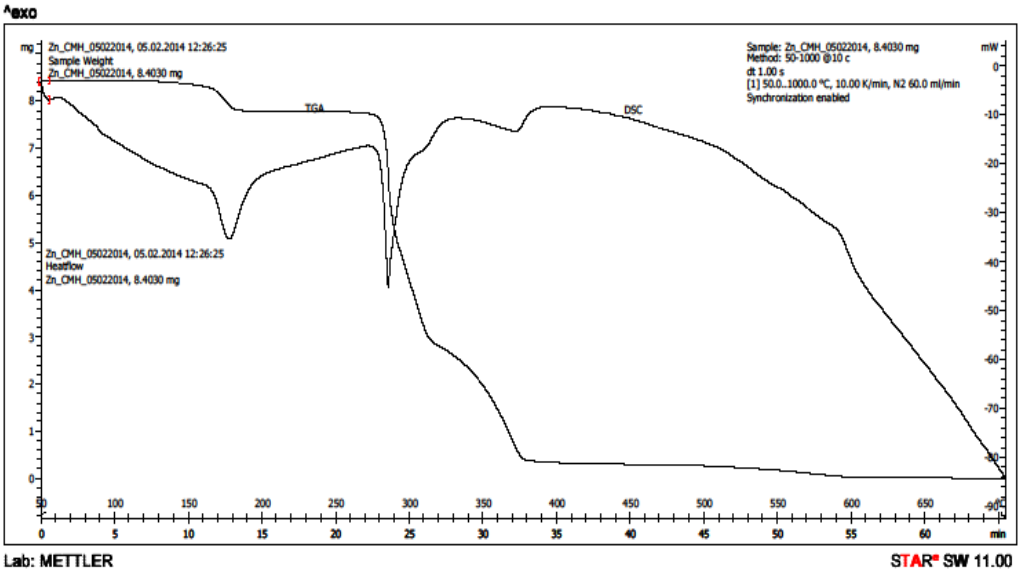

Fig 1: Zn-KYNA

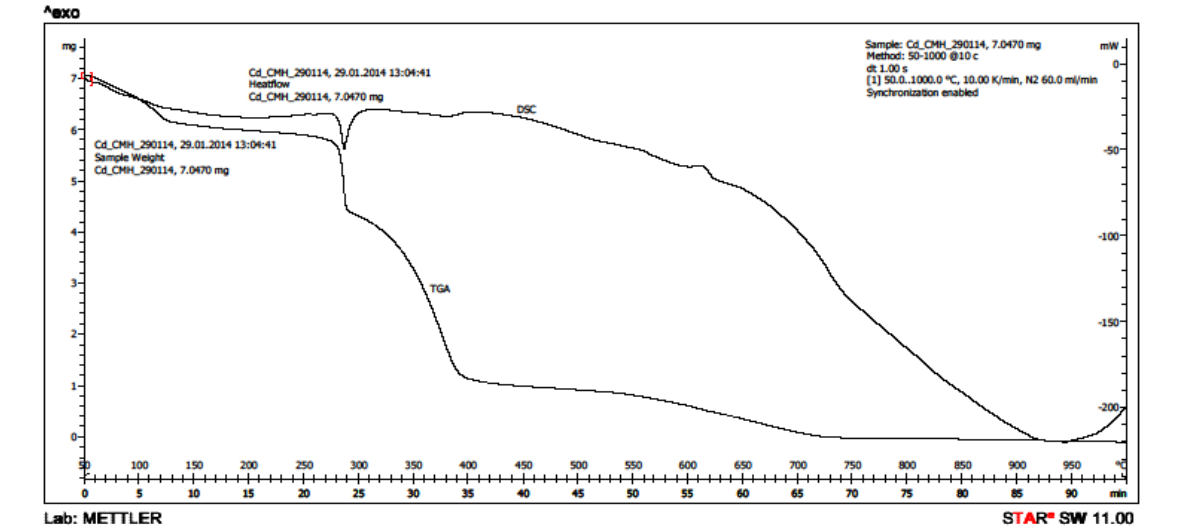

Fig 2: Cd-KYNA

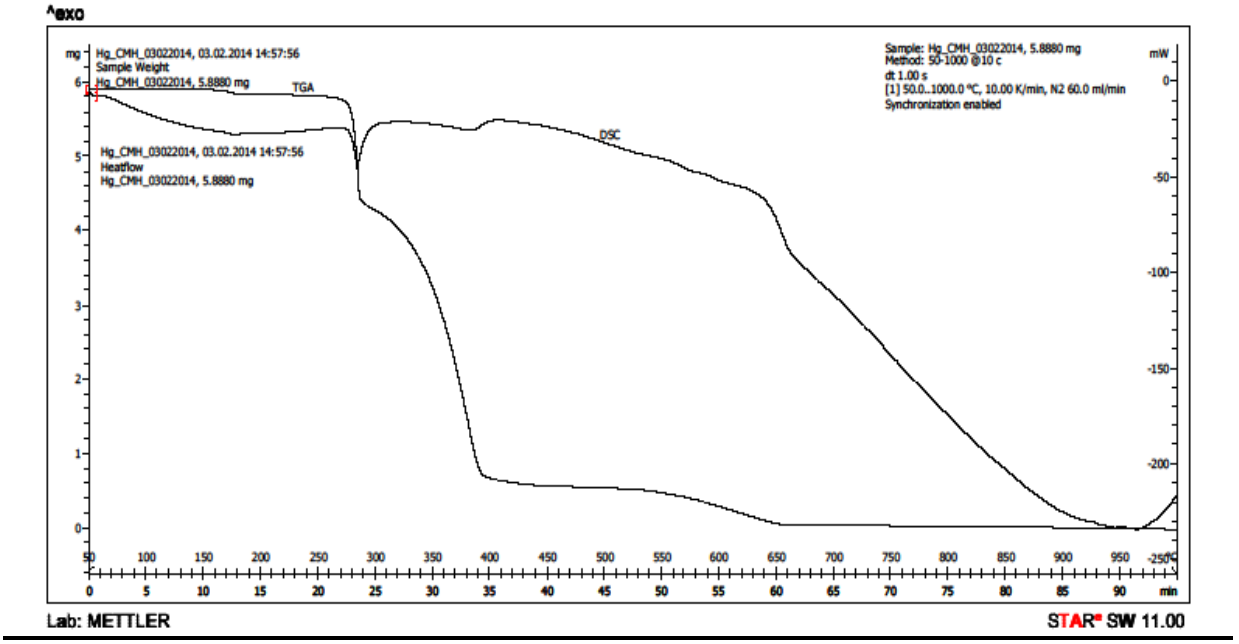

Fig 3: Hg-KYNA

It is observed that at 150^{0}C temperature in Zn-KYNA complex 4.0 gm weight loss per mole occurred , which indicates that no H_2O molecule of crystallization with Zn-KYNA is present and at the 250^{0}C temperature 39.43 gm weight loss occurred for one mole zinc complex which indicates that two water molecules with Zn^{2+}complex.
Thermo gravimetric analysis for one mole of Cd-KYNA at 150^{0}C temperature, 69.57 gm weight loss occurred which indicated that there are four water molecules of crystallization. At 250^{0}C temperature 14.19 gm weight loss occurred by one mole complex which indicates that one coordinated water molecule is present in Cd-KYNA.
For Hg-KYNA at150^{0}C, 0.0 gm weight loss occurred which indicated that no water molecules are present as water of crystallization and at 250^{0}C temperature 8.99 gm weight loss occurred for one mole complex which indicates that practically no water molecule coordinate with Hg^{2+}metal ion.
The comparatively large disagreement between the calculated and experimental (TGA) values of metal percentage is due to small but regular weight loss observed for temperatures higher then 450^{0}C which made it practically difficult to judge oxide formation.

Table 3: Results of TGA

Compound	RT-150 ^{0}C (Water of crystallization)			150 ^{0}C – 250 ^{0}C (water of coordination)		
	% Loss	Loss of weight(gm) for 1 mole complex	water molecules	% Loss	Loss of weight(gm) for 1 mole complex	water molecules
KYNA	----	-------	----	----	--------	-----
Zn-KYNA	0.714	4.0	0	7.02	39.43	2
Cd-KYNA	13.90	69.57	4	2.83	14.19	1
Hg-KYNA	0.0	0.0	0	1.52	8.99	0

Rt= Room Temperature

RESULTS OF MASS SPECTROSCOPY

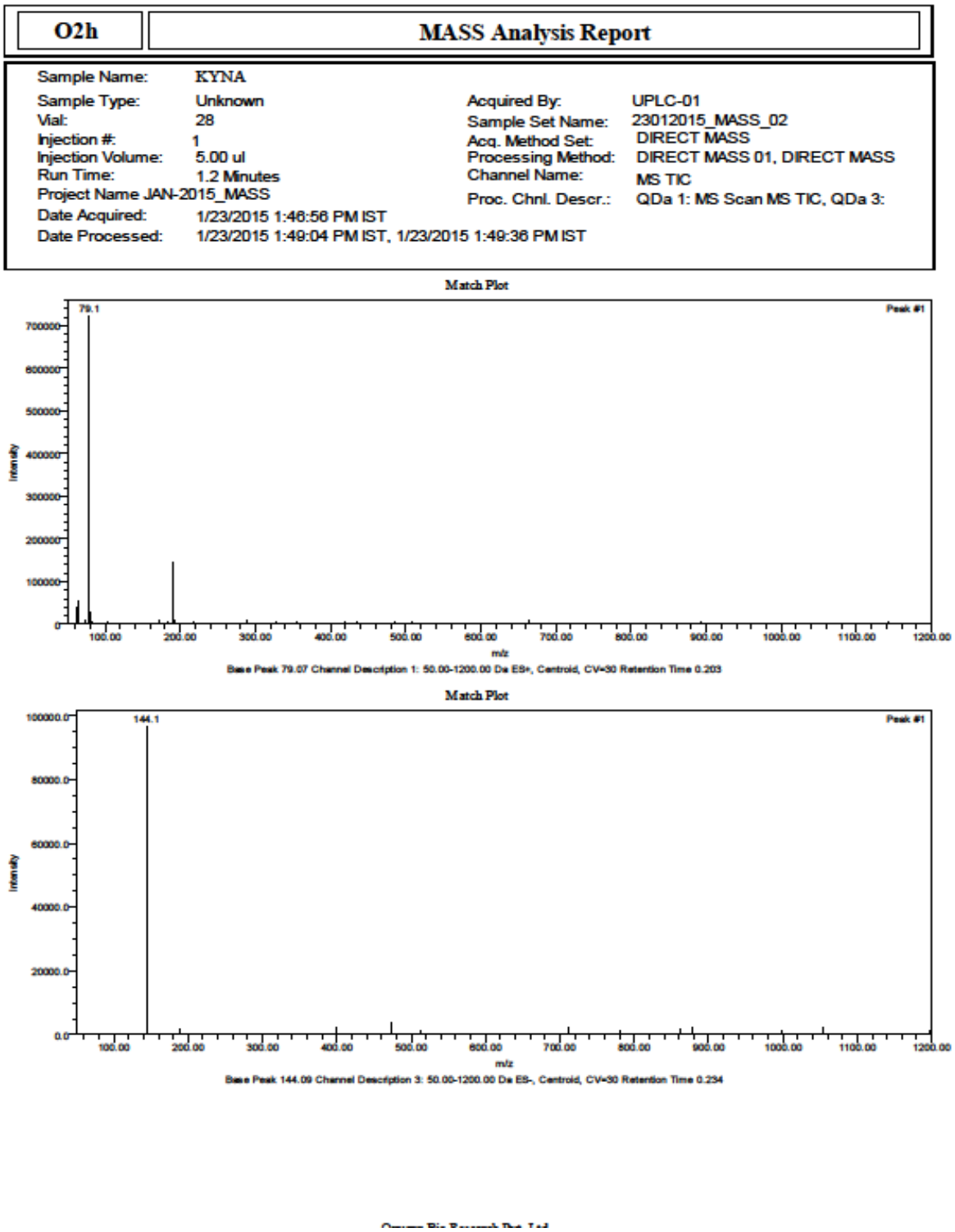

Fig 4: [KYNA mass spectra]

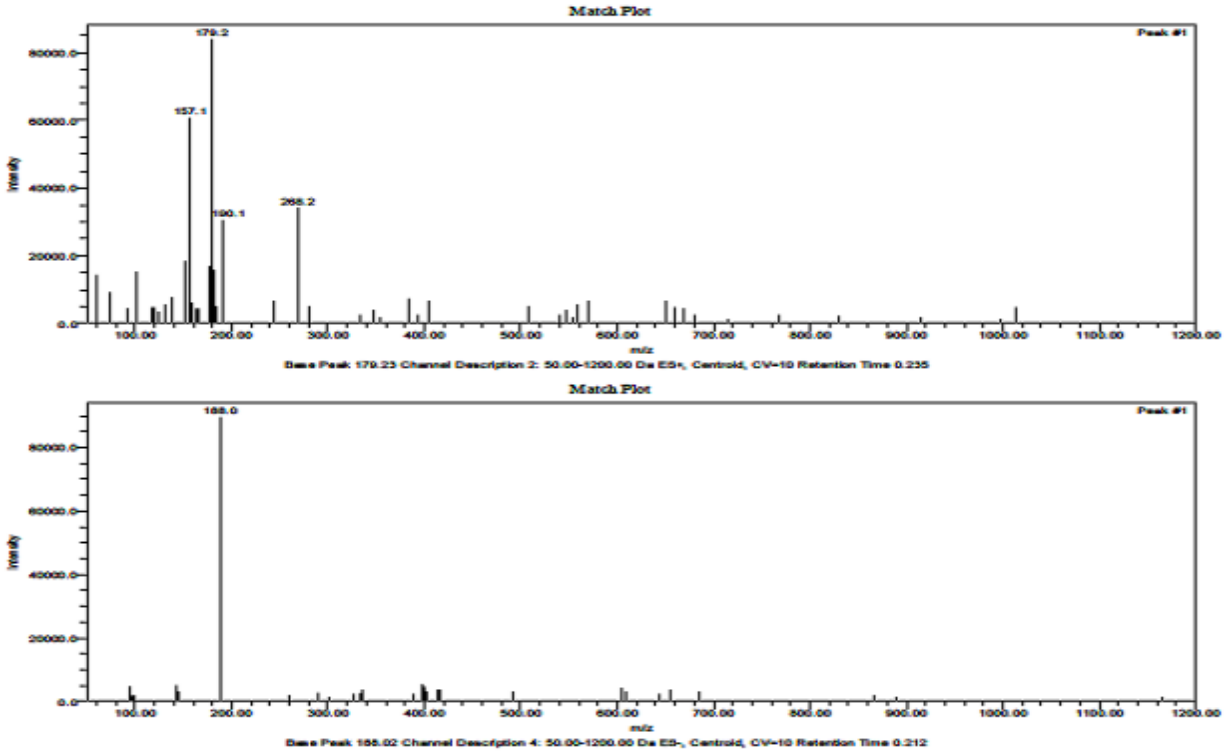

Fig 5: [Zn-KYNA mass spectra]

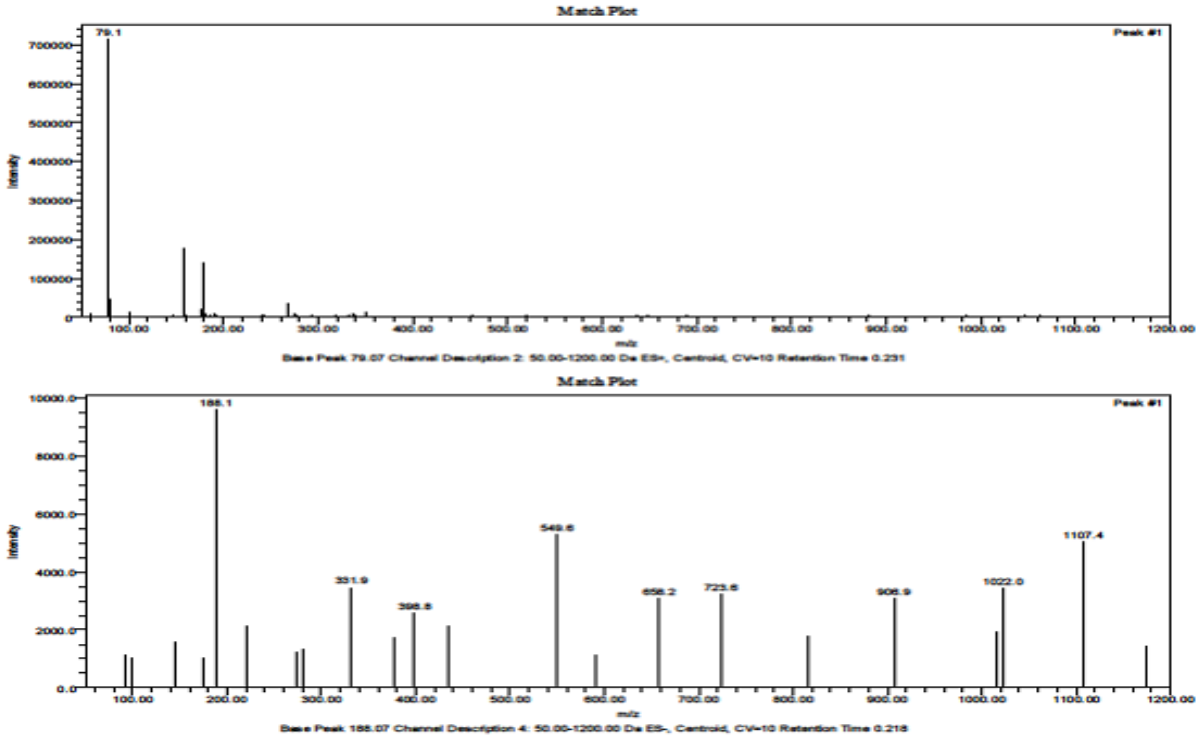

Fig 6: [Cd-KYNA mass spectra]

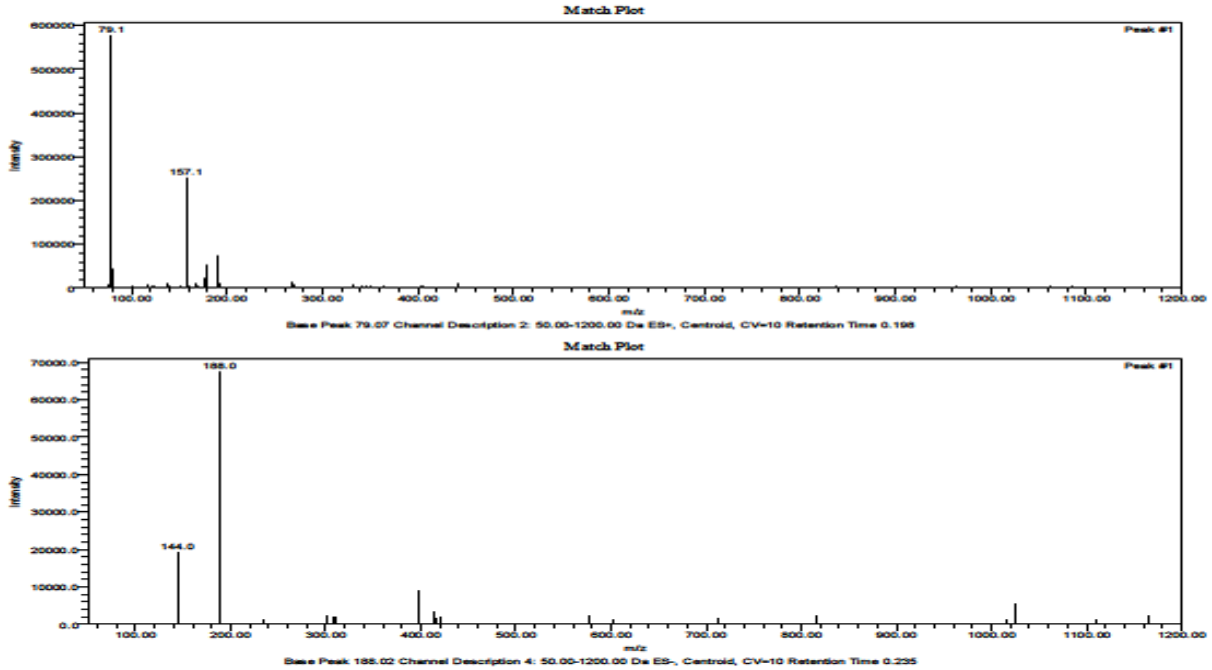

Fig 7: [Hg-KYNA mass spectra]

Mass spectra

Results for KYNA ligand

ES^+ : 189 amu is a molecular peak for $C_{10}H_8NO_3$ and 79amu is a base peak due to C_6H_6 and it is present because of removal of C_4HNO_3 from the hetero cyclic part.

ES^- : 144 amu is the base peak because of removal of –COOH group.

Results for Zn-KYNA

ES^+ : 190 amu is a M+1due to KYNA

ES^- : 290 amu is a peak for removal of one KYNA molecule from the complex.

Results for Cd-KYNA

ES^+ : 79 amu is a base peak due to C_6H_6

189 amu is a peak due to KYNA.

ES^- : 188 amu is the base peak for KYNA

144 amu peak because removal of –COOH group

Results for Hg-KYNA

ES^+ : 188 amu is the peak for KYNA

144 amu peak because of removal of –COOH group.

ES^- : 78 amu is the base peak due to C_6H_6

189 amu is the peak due to the ligand KYNA.

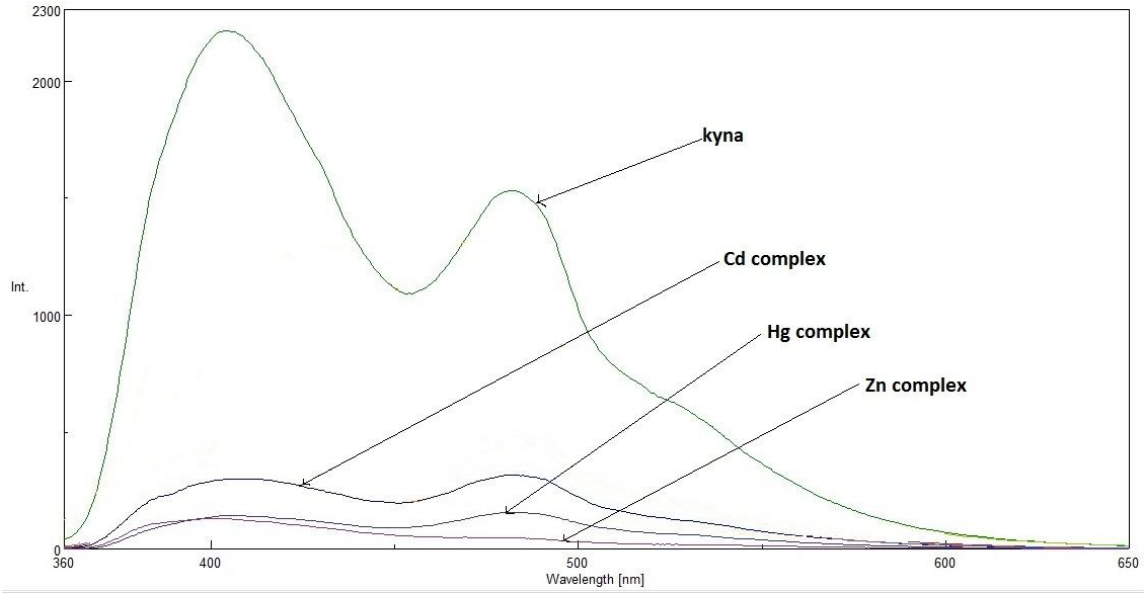

Fig 8: Fluorescence spectra: Overlapped Fluorescence spectra

Fig.8. shows the fluorescence spectra of the ligand and the complexes. The spectra is emission type spectra taken in the range of 360 nm to 650 nm. The metal ions Zn^{+2} Cd^{+2} and Hg^{+2} generally do not exhibit fluorescence activity under normal conditions. However the ligand KYNA indeed exhibits fluorescence activity, therefore it was considered to study the fluorescence behavior of the complexes. The ligand KYNA exhibits UV-visible absorption with λ_{max} below 400 nm but the fluorescence peaks around 405 nm and 480 nm. On co-ordination with the d^{10} metal ions, the fluorescence diminishes to a great extent. The order of reduction in fluorescence intensity is $Zn^{+2} > Hg^{+2} > Cd^{+2}$. The probable reason seems to be due to change in the π(pi) bonding and lone pair electron sharing for the metal coordination.

STRUCTURES

Based upon the physico chemical analyses, the structures of the three complexes can be shown as below.

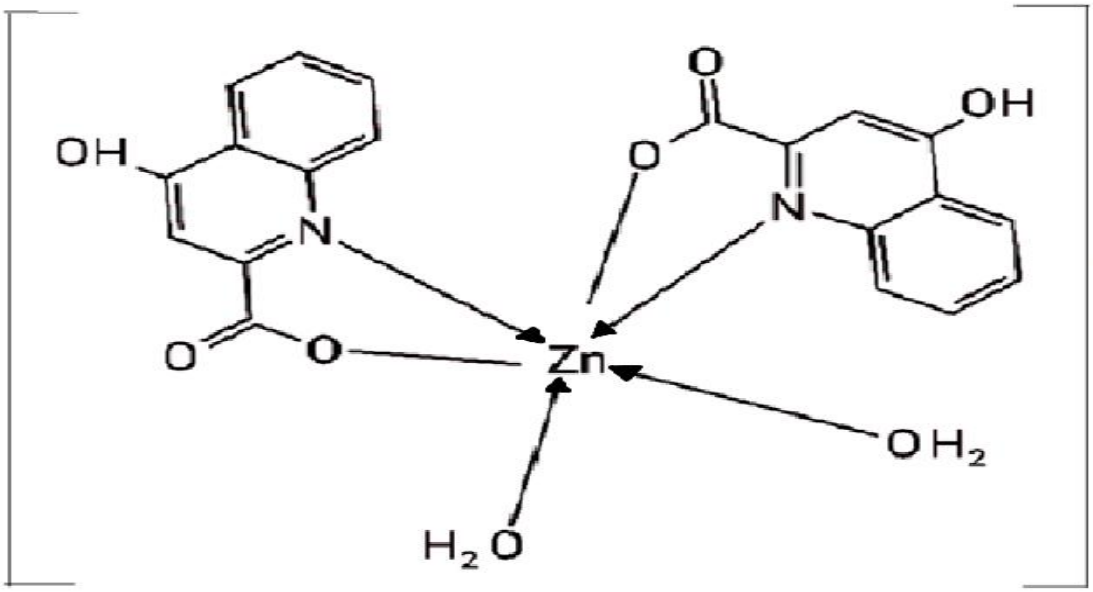

Fig 9: Zn-KYNA structure [Zn$(KYNA)_2$. 2H_2O]

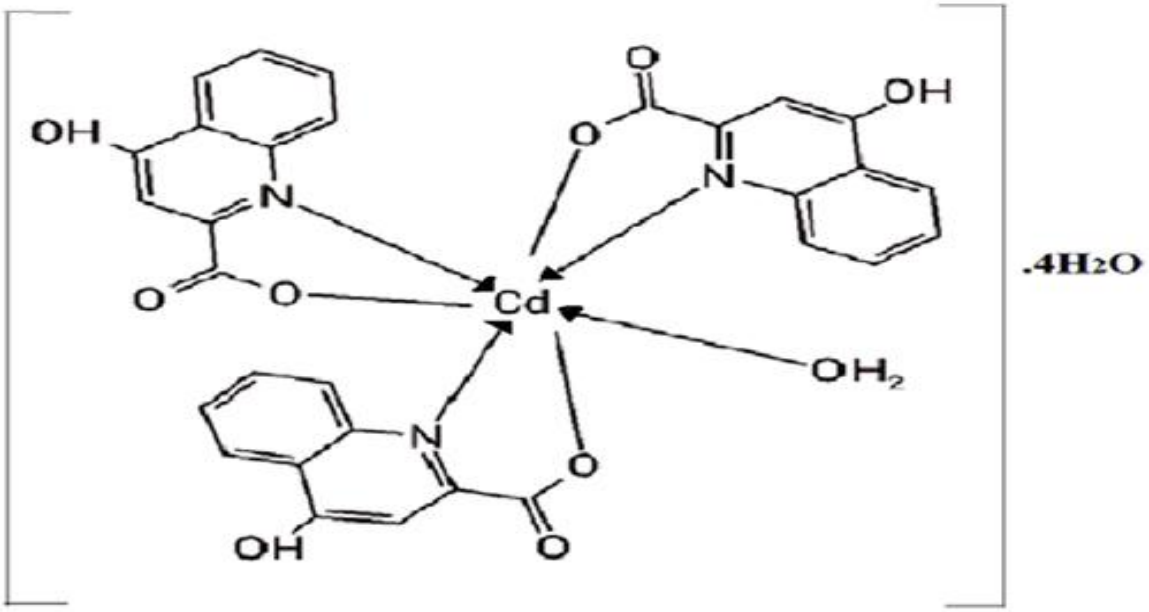

Fig 10: Cd-KYNA structure [Cd$(KYNA)_3$.H_2O]. 4H_2O

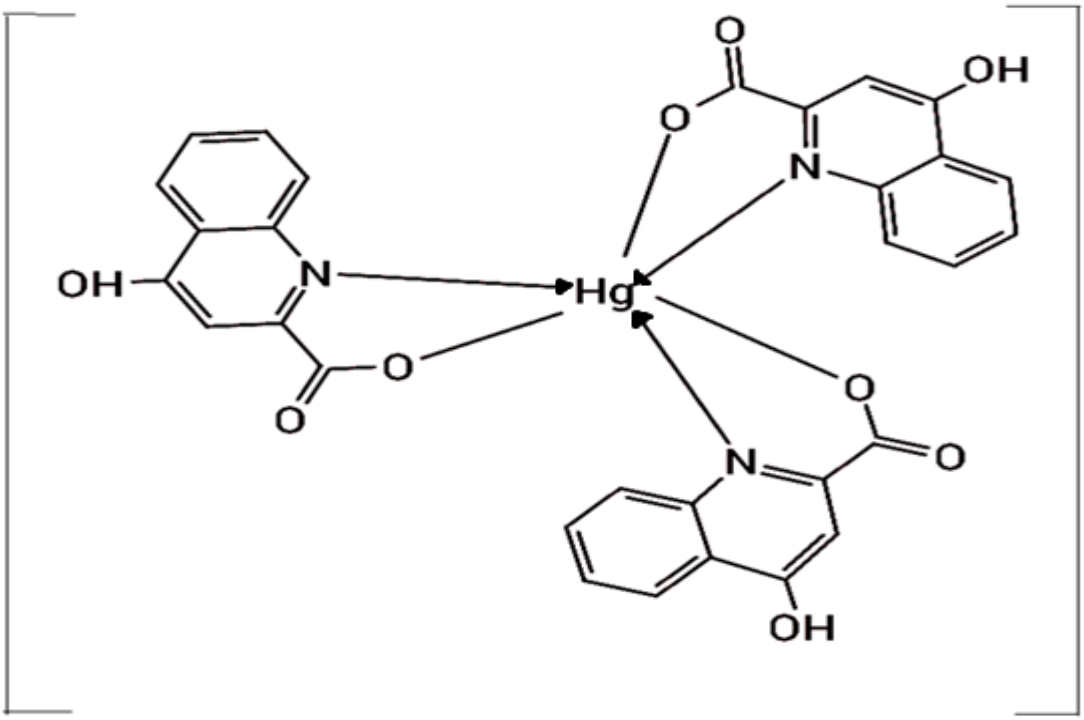

Fig 11: Hg-KYNA structure [Hg$(KYNA)_3$]

Antimicrobial activity

In vitro biological screening effects of the compounds under investigation were carried out and that was tested against the bacteria: *Salmonella typhi*, *Staphylococcus aureus*, *Escherichia coli* and *Bacillus subtilis* (Irobi, et.al., 1996). The well-diffusion method, using agar nutrient as the medium was used to check antimicrobial activity. In this method, generally compounds are loaded into well made in agar plates and their activities were tested against different organisms streaked on the surface of agar medium (Pelczar, et.al., 1993)

The stock solution of compounds (10^{-2} M) was prepared by dissolving the compounds in DMSO.The given cultures were streaked on agar plates and well were made with the help of cork borers. The well was filled with the test solution using a micropipette and the plate was incubated 24 h for bacteria at 35°C. During this period, the test solution diffused and the growth of the inoculated microorganisms was affected. The inhibition zone was developed, at which the concentration was noted (Raman, et.al., 2007)

Standard Antibacterial

Zone size	Antimicrobial disc used in practical
+++ 2.6 to 3.0 cm	Streptomycin (25µg/disc) for E-coli, S.typhy and S. aureus
++ 2.0 to 2.5 cm	Ampicilin (25µg/disc) for Bacillus sp.
- No zone 0.8 cm	

All antibiotics in standard condition gave +++ results.

Table 4: Results of Antibacterial Studies

Culture	Well no.	Compound			
		Zn complex	Cd complex	Hg complex	KYNA
Bacillus subtilis (Gram-possitive)	1. 25 mcg/ml	+	+	+	+
	2. 50 mcg/ml	+	+	+	+
	3. 75 mcg/ml	+	+	+	++
	4. 100 mcg/ml	+	++	+	+++
Staphylococcus aureus (Gram-possitive)	1. 25 mcg/ml	_	_	_	_
	2. 50 mcg/ml	_	_	_	_
	3. 75 mcg/ml	_	_	_	+
	4. 100 mcg/ml	++	+	_	++
Escherichiacoli (Gram negative)	1. 25 mcg/ml	_	_	+	_
	2. 50 mcg/ml	_	_	+	+
	3. 75 mcg/ml	_	_	+	_
	4. 100 mcg/ml	_	++	++	_
Salmonellatyhi A (Gram negative)	1. 25 mcg/ml	_	_	_	_
	2. 50 mcg/ml	_	_	_	_
	3. 75 mcg/ml	_	_	_	_
	4. 100 mcg/ml	_	_	_	_

The KYNA has inhibitory effect on gram +ve bacteria namely Bacillus, Staphylococcus but no inhibitory effect on gram –ve cultures. Zn-KYNA, Hg-KYNA showed decreased inhibition on gram +ve bacteria. Hg-KYNA, Cd-KYNA derivatives showed inhibitory effect on E coli at 100 mcg/ml concentration. The ligand and complexes did not exhibit any inhibitory effect on gram negative bacteria in general. Hg-KYNA showed some inhibitory effect against E-coli as the metal mercury has important antimicrobial activities. Another observation was that on coordination of KYNA, the overall antibacterial activity decreased. The antibacterial activity of ligand and complexes was much less compared to the standard antibiotics selected.

CONCLUSION

The KYNA ligand was selected due to its important biological role and d^{10} metal ions were selected because of their typical physiological activities. Different physico chemical techniques confirmed coordination with octahedral- six coordinate structures Zn, Cd and Hg complexed with 2,3 and 3 ligand molecules respectively. On complex formation, fluorescence of ligand decreased as well as overall reduction in antimicrobial activity was noted.

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