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Biospecific activities of rare earth complexes of hippuric acid and sulfanilamide

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ABSTRACT

The stability constants of some biospecific ligands (BHEB, BHETB, BHEAB) with the lanthanide ions determined potentiometrically reveals that the ligands have protons to dissociate and complexation occurs. The stability of metal complexes is expected to follow the order : Pr (III) < Nd (III) < Sm(III) < Gd (III) < Tb (III) < Dy (III) < Er (III). The complexes show antifungal and antioxidant activities.

Keywords : Hippuric acid, 4-amino benzene sulfonamide, 4-amino-N-2-thiazolyl-benzene sulfonamide, N-(4-amino benzene sulfonyl) acetamide, stability constants, IR, Electronic, Thermal, Magnetic, Antifungal, Antioxidant.

INTRODUCTION

MAOS (Mircrowave Assisted Organic Synthesis) strategies coupled with solvent free reaction chemistry offer feasible solutions as their benefits are manifolds. They frequently leads to dramatically reduced reaction times, higher yields, cleaner reaction profiles and above all eco-friendliness. As our interest in "search for bioactive heterocycles" we sought unexplored, synthetically accessible heterocyclic chelates which are capable of bearing some potential pharmacophores to elicit and enhance the inherent biological activity. A number of compounds are found to be endowed with special therapeutic activities such as antitumor[1], antiviral[2],antimycobacterial[3], antifolate[4], antiproliferate[5], antihistaminic[6] etc. With this endeavour, number of polychelates showing characteristics like strong bonds, multiple valencies for the attachment of wide variety of other groups, high thermal stability and ability to tailor new, interesting and fascinating structures with endless variations were synthesized with nitrogen, oxygen and sulphur in their environment.

The ionic radii of trivalent lanthanide ions make them easily available for complexation. As higher charge / radius leads to stronger electrostatic bonding. Secondly, the lanthanide ions have a larger hydration sphere and lastly, replacement of any water molecule by another group or molecule of ligand increases the entropy of the system, which in turns results in higher stability constants.

The metal chelates depending on their structures with endless variations can be used as catalyst, high temperature and flame resistant fibres, semiconductors, ion-exchange resins, for agricultural purpose and most important their use in fabrication of polymer light emitting diodes to enable low cost, full colour and flat panel display[7-9].

MATERIALS AND METHODS

The lanthanide (III) chlorides /nitrates were obtained from Rare Earth Products Ltd. (India) and were used without further purification. The solutions were acidified with accurately known amounts of HNO_3 to prevent hydrolysis. The ligands **(1-3)** were synthesized both by microwave and conventional methods. The purity of these compounds were confirmed by TLC, NMR, IR and melting points.

Ligands 1, 2, 3 [BHEB, BHETB, BHEAB] : Mixtures of Benzoyl amino acetic acid (0.01 mole) and 4-amino benzene sulfonamide (0.01 mole), 4-amino-N-2-thiazolyl-benzene sulfonamide (0.01 mole), N-(4-amino benzene sulfonyl) acetamide (0.01 mole) and sodium ethoxide were microwave irradiated for about 3-8 min. Resulting products were poured onto crushed ice and were filtered and dried. Similarly the compounds were refluxed for 8-12 hrs, [9] corresponding solvents were distilled off and the reaction mixtures were collected and crystallized from methanol. Satisfactory results of yield and analytical parameters were obtained.

The stepwise dissociation constant of the ligands at a definite ionic strength (μ=0.1M $NaClO_4$) were calculated and the formation curves were plotted.

Ligands **(1-3)** coordinates to metal ions which reveals that complexation is a proton-releasing reaction.

RESULTS AND DISCUSSION

The extent of deviation may be the dissociation of – OH group. The ligands **(1-3)** may be considered as monobasic acid having one replaceable H^+ ion from phenolic – OH group and can be represented as $-HL \leftrightarrows H^+ + L^-$;

Protonation Constants :	L_1	L_2	L_3
Log K_1^H :	9.52	9.98	10.40

A linearity was observed between log K_1^H and 100/D.

M-L STABILITY CONSTANT (Log K):
Values of log k_1 & log k_2 indicates the stepwise formation of complexes between the metal ions and the ligands. When plotted against Z^2/r of lanthanide ions, linearity was observed.

The magnetic moment value (Table – 1) reveals the diamagnetic nature of the La-complexes, as expected from its closed shell electronic configuration and absence of unpaired electrons, where as all other ions are paramagnetic due to the presence of 4f electrons, which are effectively shielded by $5s^2$ $5p^6$ electrons.

SPECTRAL:
IR: Distinct values were obtained for azomethine and hydroxyl group, which were found to be influenced on complexation[10].

ELECTRONIC: La (III) has no significant absorption but for other ions, transitions from ground level $^3H_4$, $^4I_{9/2}$, $^6H_{5/2}$, $^8S_{7/2}$ and $^6H_{15/2}$ to excited J-levels of 4f configurations are observed [11-12]. Red shift or nephelauxetic effect is also observed, indicating the covalency in these complexes.

THERMAL:
Careful analysis of pyrolysis curve reveals that the complexes do possess water of crystallization. From 220^{o}c, compounds started losing mass due to partial evaporation of organic ligand upto 290^{o}c. Residues were obtained after heating upto 850^{o}c and are expected to be close to lanthanide oxides [13].

FUNGICIDAL ACTIVITY:
The ligands and their complexes were screened for their antifungal activities against *Candida albicans*, *Candida krusei*, *Candida glabrata* and *Aspergillus fumigatus*. Complexes were found to be fungi toxic in nature, though the activity was found to be not so good. Yet can serve as a vechicle for activation of ligands as principle cytotoxic species[14].

ANTIOXIDANT ACTIVITY :

The synthesized compounds were tested for their *in vitro* antioxidant activity by 1,1-diphenyl-2-picry1hydrazyl(DPPH) method. The free radical scavenging potentialities of the compounds were measured in terms of hydrogen donating or radical scavenging ability using 1ml [(methanolic solution of DPPH(0.1 mm)] which was added to 3ml of sample solution in methanol at different concentrations(10-40 µg/ml). Test compound reacts with DPPH and degree of decolourization indicates the scavenging potentialities of the antioxidant drug. The change in the absorbance produced at 520nm has been used as a measure of antioxidant activity [15]. Scavenging activity was expressed as:

$$\text{DPPH Scavenged (\%)} = \frac{(A_{cont}-A_{test})}{A_{cont}} \times 100$$

TABLE – 1 Physical and analytical parameters of the ligands (BHEB, BHETB, BHEAB) and their complexes

Ligands/ Complexes	Colour	M.P. (^{o}c)	Yield(%)		Microwave Time (sec.)	Thermal Duration (hrs.)	Elemental Analysis% found(calc.)						
			Microwave	Thermal			C	H	N	O	S	M	µ(B.M.)
L_1	Light Brown	145	78	52	5.0	8.0	53.3 (54.0)	3.9 (4.5)	11.9 (12.6)	18.7 (19.2)	9.1 (9.6)	-	-
L_2	Green	110	82	56	7.5	7.5	51.6 (52.1)	2.7 (3.3)	12.8 (13.5)	15.0 (15.4)	14.8 (15.4)	-	-
L_3	Dark brown	105	91	65	8.0	6.5	53.8 (54.4)	3.8 (4.5)	10.5 (11.2)	20.5 (21.3)	8.1 (8.5)	-	-
L_1-La	Brown	280	78	55	6.0	7.0	37.3 (38.1)	2.5 (3.1)	8.2 (8.9)	13.0 (13.5)	6.0 (6.7)	29.4 (28.6)	Dia
L_1-Pr	Blackish Brown	270	70	48	7.0	9.0	37.1 (37.9)	2.4 (3.1)	8.1 (8.8)	12.9 (13.5)	6.1 (6.7)	29.1 (29.7)	3.60
L_1-Nd	Greenish brown	272	75	60	7.0	6.0	37.0 (37.7)	2.2 (3.1)	8.1 (8.8)	12.8 (13.4)	6.2 (6.7)	29.5 (30.2)	3.59
L_1-Sm	Black	278	82	40	7.0	5.0	36.5 (37.2)	2.4 (3.1)	7.9 (8.6)	12.5 (13.2)	6.1 (6.6)	30.4 (31.1)	1.68
L_1-Gd	Light Brown	282	80	57	6.5	7.0	36.1 (36.7)	2.4 (3.0)	7.8 (8.5)	12.2 (13.0)	5.8 (6.5)	31.1 (32.0)	7.92
L_1-Tb	Blackish Brown	279	75	59	6.0	7.5	36.0 (36.5)	2.2 (3.0)	7.9 (8.5)	12.3 (13.0)	5.7 (6.5)	31.6 (32.3)	9.50
L_1-Dy	Greenish Brown	265	72	60	9.0	7.0	35.2 (36.3)	2.3 (3.0)	7.8 (8.4)	12.3 (12.9)	5.5 (6.4)	32.1 (32.7)	10.60
L_1-Er	Black	275	79	62	8.5	8.0	35.2 (35.9)	2.1 (2.9)	7.7 (8.3)	12.1 (12.7)	5.8 (6.3)	32.8 (33.4)	10.75

TABLE – 2 STABILITY CONSTANTS OF THE RARE EARTH COMPLEXES AT 25^{o} c AND I = 0.1 M

La – $L_1/L_2/L_3$	11.00, 11.10, 11.15
Pr – $L_1/L_2/L_3$	11.45, 11.42, 11.52
Nd – $L_1/L_2/L_3$	11.62, 11.70, 11.65
Sm – $L_1/L_2/L_3$	12.00, 12.10, 12.25
Gd – $L_1/L_2/L_3$	12.15, 12.18, 12.28
Tb – $L_1/L_2/L_3$	12.48, 12.55, 12.65
Dy – $L_1/L_2/L_3$	12.85, 12.90, 12.91
Er – $L_1/L_2/L_3$	12.95, 13.05, 13.20

TABLE – 3 ANTIOXIDANT ACTIVITY

Compounds	Percentage of radical scavenging activity (%)			
	10µg/mL.	20µg/mL.	30µg/mL.	40µg/mL.
L_1-La	11.0	8.9	11.5	11.2
L_1-Pr	10.1	15.1	12.1	14.1
L_1-Nd	13.1	13.4	15.2	16.1
L_1-Sm	6.7	8.3	8.8	12.2
L_1-Gd	10.1	9.3	7.1	8.4
L_1-Tb	12.4	10.1	8.9	12.2
L_1-Dy	9.2	10.1	8.2	11.1
L_1-Er	12.1	13.0	11.1	10.3

CONCLUSION

Metal complexes are found to posses antioxidant and good antifungal activity, though of weak intensity.

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REFERENCES

[1] P.G. Baraldi, M.G. Pavani, M. Nunez, P. Brigidi, B. Vitali, R. Gambari and R. Romagnoli, *Bio Org Med Chem*.**, 2002,**10, 449.
[2] M.N. Nasir and M.M. Gineinalh, *Arch Pharm***, 2002,** 335**,** 289.
[3] A. Kumar, S. Sinha and M.S. Chouhan, *Bio Org Med Chem Lett***., 2002,**12, 667.
[4] A. Gangjee, A. Vidwans, E. Elzein, S.F. Queener and R.L. Kislink, *J Med Chem.,* **2001,** 44**,** 1993.
[5] N. Kumar, G. Singh and A.K. yadav, *Hetero atom Chem*.**, 2001**, 12, 852.
[6] J. Griffon, J.A. Montgomary and J.A. Secrist, *Nucleosides and Nucleostives***, 2001**,20, 649.
[7] E. Butter, Chem Abst. **1972,** 77**,** 830.
[8] R.K. Agarwal and B. Prakash, *Transition Met Chem***., 2005,** 30**,** 696.
[9] A.S. Aswar, A.D. Bansood and P.R. Mandik, *Ind J Chem*.**, 2004,** 43A, 1892.
[10] L.J. Bellamy**,** *Infared Spectra of Complex Molecules***,** Methun, London **1954**.
[11] S.P. Tandon and P.C. Mehta, *J Chem Phys***, 1970,** 52, 4313.
[12] R.K. Agarwal and R.K. Sarin, *Polyhedron***, 1993,** 13**,** 2411.
[13] R.K. Agarwal and S.K. Gupta, *Polish J Chem*.**, 1987,** 61**,** 341.
[14] J. Singh, R. Vohra and D.K. Sahoo, *J Ind Microbial Biotechnol***, 2001,** 2**,**387.
[15] S.J. Wadher, A.R. Tapas and P.G. Yeole, *Int. J. Chem. Sci***, 2006,** 4**,** 761.