Electronic Spectral Characterization of Pr(III) Antibiotic Complexes in Solution

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The present work involves the study of some Pr (III)-antibiotic complexes in 50 % DMSO-H_2O composition. The ligands included five antibiotics (ceftizoxime, pipercillin, cefuroxime, cefotaxime and cefazolin). The effect of the ligand environment on electronic spectra of the metal ion with special reference to complexation and nature of metal-ligand bond has been investigated. Various energy parameters *i.e.*, [Slate-Condon (F_k), Racah (E^k) and Lande parameter(ζ_{4f})], bonding parameter ($b^{1/2}$), Nephelauxetic ratio (β)] and intensity parameters [oscillator strength (P), Judd-Ofelt parameter (T_λ)] had been evaluated for different metal ligand stoichiometries.

Key Words: Pr(III), Antibiotics, Electronic spectra, Energy parameters, Intensity parameters.

INTRODUCTION

Biomolecular systems are consisting of excellent bonding sites to fulfill the coordination requirements of lanthanide complexes. A wide variety of lanthanide complexes with these types of compounds have been prepared and studied to find out the fundamental nature of the complexes. A perusal of the literature shows remarkable use of lanthanide complexes in the production of pharmacologically important compounds. The photoactivatable lutetiumanalogue motexafin lutetium is being investigated as photo therapy for vulnerable atheroselerotic plaque[1].

The recent success story for lanthanides as therapeutic metals has been the approval for lanthanum carbonate fosrenol, as phosphate binder for the treatment of hyperphosphatemea in renal dialysis patients in both USA and Europe[2,3]. Efficacy and safety have been demonstrated in several phase III clinical trials in both Europe and North America[4]. The lanthanides have been reported to inhibit lymphocyte activation, neutrophil chemotaxis and aggregation[5,6]. These complexes have found a role in cancer treatment as contrast imaging agents such as Gd(III) DTPA which is commonly used for MRI of tumors[6-8]. A more recent investigational drug is the redox active lanthanide texaphyrin complex, motexafin gadolinium. This is in phase III clinical trials in combination with whole body irradiation for the treatment of brain metastasizes in non small cell lung cancer[9].

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In this series, we tried to prepare praseodymium(III) antibiotic complexes which are supposed to increase efficiency of the drug taken.

EXPERIMENTAL

Pr_4O_{11} used in this study was of analytical grade, purchased from Loba. All the antibiotics were purchased from Lupin. DMSO of Merck was used as solvent. The praseodymium chloride used was prepared from its oxide by dissolving it in minimum amount of 50 % HCl. The salt was recrystallized by evaporating the resulting solution over water bath and dried under vacuum over P_4O_{10}. The prepared salt is hygroscopic in nature so it was kept in a desiccator with a strong dehydrating agent. 0.05 M stock solution was prepared by dissolving ligand in 50 % DMSO. The above chemicals were used as such, without further purification. All prepared solutions were standardized by conventional methods[10,11].

The experimental procedure used by earlier workers[12,13] was followed for the present work. The metal ion and ligand solutions were mixed in 1:1, 1:2, 1:3 and 1:4, ratio. The pH of the above systems were adjusted between 6 and 7, immediately after mixing the metal ion and ligand solution, by gradual addition of dil. NaOH or dil HCl. All the above systems were kept for 1 h to attain equilibration. The spectra of above systems were recorded in UV-visible region.

RESULTS AND DISCUSSION

From all the observations it has been found that 1:2 metal ligand stoichiometry, as obtained in most of lanthanide complexes[14-17], is the most favourable condition for the formation of lanthanide antibiotic complexes. Therefore all the spectral parameters discussed here are at 1:2 M-L stoichiometry. The UV-vis absorption bands of Pr(III), systems were observed (Table-1) in the region of 400-600 nm due to the *f-f* transition consisting $^3H_4 \rightarrow D_2$, $^3H_4 \rightarrow {}^3P_0$, $^3H_4 \rightarrow {}^3P_1$, $^3H_4 \rightarrow {}^3P_2$ multiplets.

The treatment of results obtained in the spectral studies, was based on the calculation of various intensity and energy parameters as well as on the application of various theories proposed for the spectral behaviour of lanthanide complexes.

Intensity parameters: These parameters include oscillator strength and Judd-Ofelt intensity parameters[18,19]. The measured intensity of an absorption band is related to the probability of radiant energy by the expression:

$$P_{obs} = 4.6 \times 10^{-9} \times \in_{max} \times \Delta \nu_{1/2}$$

where $\in_{max}$ = molar extinction coefficient of the peak maximum and $\Delta \nu_{1/2}$ is half intensity band width.

The calculated oscillator strength is represented in terms of T_2, T_4 and T_6 parameters as

$$P_{obs} = [T_2[U^2]^2 + T_4[U^4]^2 + T_6[U^6]^2]\,\overline{\nu}$$

The values of $[U^2]^2$, $[U^4]^2$ and $[U^6]^2$ have been taken as reported by Carnall *et al.*[20] and T_2, T_4 and T_6 are Judd-Ofelt intensity parameters (Table-2).

TABLE-1
OBSERVED AND CALCULATED VALUES OF OSCILLATOR
STRENGTH AND ENERGIES OF Pr(III) ANTIBIOTIC COMPLEXES

Ligand	Energy (cm^{-1})	Energy levels				
		$^1D_2$	$^3P_0$	$^3P_1$	$^3P_2$	σ_{rms}
Ceftizoxim	E_{exp}	16954.89	20733.98	21358.39	22527.59	
	E_{cal}	16959.76	20736.81	21365.43	22536.77	6.44
	$P_{exp} \times 10^6$	2.21	3.33	5.91	13.05	
	$P_{cal} \times 10^6$	0.51	4.38	4.45	14.15	0.7271×10^{-6}
Piperacillin	E_{exp}	16806.72	20678.25	21240.44	22396.42	
	E_{cal}	16843.5	20696.36	21298.05	22474.29	53.03
	$P_{exp} \times 10^6$	3.93	2.97	3.25	12.79	
	$P_{cal} \times 10^6$	2.25	2.88	2.92	13.71	0.4594×10^{-6}
Cefuroxime	E_{exp}	16954.89	20622.81	21299.25	22461.81	
	E_{cal}	16953.8	20622.8	21297.01	22457.8	2.094
	$P_{exp} \times 10^6$	4.02	3.53	4.61	11.97	
	$P_{cal} \times 10^6$	2.47	3.84	3.92	12.726	0.378×10^{-6}
Cefotaxim	E_{exp}	16809.55	20682.52	21244.95	22401.43	
	E_{cal}	16846.31	20700.52	21301.84	22478.11	0.9465
	$P_{exp} \times 10^6$	3.5	3.43	3.87	1.12	
	$P_{cal} \times 10^6$	2.07	3.46	3.50	11.88	0.38×10^{-6}
Cefazolin	E_{exp}	16917.61	20678.25	21299.25	22461.81	
	E_{cal}	16932.49	20685.84	21321.93	22492.13	20.17
	$P_{exp} \times 10^6$	3.41	3.39	3.62	10.47	
	$P_{cal} \times 10^6$	2.06	3.32	3.38	11.16	0.345×10^{-6}

TABLE-2
INTENSITY PARAMETERS OF Pr(III) ANTIBIOTIC COMPLEXES

Ligand	$T_2 \times 10^9$ (cm)	$T_4 \times 10^9$ (cm)	$T_6 \times 10^9$ (cm)	T_4/T_6	O.S. of Hypersensitive peak $P_{obs} \times 10^6$	$\nu T_6 \times 10^6$	$K = P_{obs}/\nu T_6$
Ceftizoxime	-30.49	1.474	4.797	0.3072	14.92	107.749	0.1385
Pipercillin	-47.61	1.625	4.390	0.3701	13.67	98.607	0.1386
Cefuroxime	-84.57	1.221	4.411	0.2768	13.05	99.366	0.5790
Cefotaxime	-39.93	0.805	4.302	0.1870	12.79	96.349	0.1327
Cefazolin	-28.81	1.078	3.893	0.2770	11.97	87.443	0.1368

The values of both the oscillation strength *i.e.*, P_{exp} and $P_{cal.}$ are nearly identical. The low value of σ_{rms} deviation indicates the applicability and suitability of Judd-Ofelt theory. The negative value of T_2 was found for Pr (III) systems. The behaviour may be due to one or more of the following[21] points. Strong f-d mixing: poor resolution method of the overlapped 3p-bands; small number of observed or fitted lines; or due to using incorrect value of reduced matrix elements of Pr(III). The ratio of T_4/T_6 showed smaller change, thereby suggesting that symmetry changes are less prominent. The value of νT_6 is found directly proportional to the intensity of hypersensitive transition which indicates the dependence of intensity on covalency. The

increase in intensity is in the order ceftizoxim > piperacillin > cefuroxime > cefotaxim > cefazolin, which is relevant to the steric effects of the ligands.

Energy parameters: These parameters give useful information regarding to interelectronic repultion, spin-orbit interaction, nephelauxetic effect and bonding in complexes. Energy parameters consist following parameters.

Slator-Condon F_K (K = 0, 2, 4, 6): The Slator integrals[22,23] are expressed in terms of Slator-Condon (Table-3). Parmaeters (F_K) by following relations:

$$F_2 = F_2/225$$
$$F_4 = F_4/1089$$
$$F_6 = F_6/7361.64$$

Lande parameters (ζ_{4f}): Employing a least squares fit method, correction factors ΔF_2, ΔF_4, ΔF_6 and $\Delta\zeta_{4f}$ are obtained The Slater-Condon (F_2, F_4, F_6) and the spin orbit $\Delta\zeta_{4f}$ parameters are obtain from following relation (Table-3).

$$\Delta F_2 = F_2 - F_2°$$
$$\Delta F_4 = F_4 - F_4°$$
$$\Delta F_6 = F_6 - F_6°$$
$$\Delta\zeta_{4f} = \Delta\zeta_{4f} - \Delta\zeta°_{4f}$$

where $F_2°$, $F_4°$, $F_6°$ and $\zeta°_{4f}$ are the zero order parameters.

TABLE-3
ENERGY PARAMETERS OF Pr(III) ANTIBIOTIC COMPLEXES

Ligand	E^1	E^2	E^3	F_2	F_4	F_6	F_2 (%)	F_4/F_2	F_6/F_2	ζ	ζ (%)	β	$b^{1/2}$
Ceftizoxime	4221.05	25.15	458.20	305.67	36.38	4.08	5.09	0.119	0.0133	729.46	1.55	0.9490	0.1596
Pipercillin	4608.60	22.07	457.86	304.80	46.37	4.71	5.36	0.152	0.0154	712.30	3.87	0.9463	0.1638
Cefuroxime	3552.05	29.43	455.11	303.97	20.08	3.02	5.62	0.066	0.0099	732.58	1.13	0.9437	0.1677
Cefotaxime	4614.99	22.04	457.95	304.86	46.50	4.71	3.04	0.152	0.0154	712.70	3.81	0.9465	0.1635
Cefazolin	4109.09	22.68	957.07	304.98	33.75	3.91	5.31	0.110	0.0128	724.20	2.22	0.9468	0.1629

Racah parameters E^K (k = 1, 2, 3): The electrostatic interaction is calculated in terms of Racah parameters. These are the linear combination of F_k's. They may be calculated by following relations[24,25].

$$E^1 = (70F_2 + 231F_4 + 2002F_6)/9$$
$$E^2 = (F_2 - 3F_4 - 7F_6)/9$$
$$E^1 = (5F_2 + 6F_4 - 91F_6)/3$$

Nephelauxetic ratio (β): Nephalauxetic ratio measures the expantion of wave function. This results in decrease of the interelectronic repulsion parameters. This parameter can be expressed as[26,27].

$$\beta = \frac{F_K}{F_K^0}$$

Here, F^C_K refers for complex and F^0_K for free ion.

Bonding parameters $b^{1/2}$: Bonding parameter[28] measured the degree of covalency and exhibit the amount of 4*f*-ligand mixing. This parameter can be given as:

$$b^{1/2} = \left[\frac{1}{2}(1-\beta)\right]^{1/2}$$

where β is nephelauxetic ratio.

The extremely low rms value of observed levels (E_{exp}) and the calculated values (E_{cal}) for Pr(III) ion with various ligands indicates the good agreement between the experimental and calculated energies as well as reproducibility of the product. F^k parameters for all the complexes under observation are found in the order: $F_2 > F_4 > F_6$ and E^K values follow the order $E^1 > E^3 > E^2$, which are in agreement with the finding of earlier workers[29-32]. There is a small decrease in value of F_2 parameters, suggesting that there is small decrease in interelectronic repulsion between $4f$ orbitals and ligand orbitals. This also indicates lower extent of complexation in lanthanide complexes as compared to transition metal complexes. The change in ζ_{4f} value on complexation is much smaller than in F^K's values. This is expected from the fact[33] that ξ_{4f} unlike F^K's is less affected by the ligand since it is mainly determined by the radial wave function of the central metal atom close to the nucleus. The values of $b^{1/2}$ are found positive and less than one, indicate the presence of covalency in metal ligand bond.

Conclusion

The results obtained are in agreement with the theories of Judd and Ofelt. The intensity aspects of lanthanide absorption spectra can be predicted to a good approximation on the basis of two parameters T_2 and T_4. The nephelauxetic ratio β and bonding parameters $b^{1/2}$ help to explain the nature of the metal-ligand bonding.

REFERENCES

1. A.M. Evens, *Curr. Opin. Col.*, **16**, 576 (2004).
2. W.F. Finn, M.S. Joy and G. Hladik, *Clin. Nephrol.*, **62**, 193 (2004).
3. W.F. Finn and M.S. Joy, *Am. J. Kidney Dis.*, **42**, 96 (2003).
4. F. Albaaj and A.J. Hutchison, *Exp. Opin. Pharmacother.*, **6**, 319 (2005).
5. K. Wang, Y. Cheng, X. Young and R. Li, *Met. Ions Biol. Syst.*, **40**, 707 (2003).
6. C.H. Evans, *Trends Biochem. Sci.*, 445 (1983).
7. A.E. Morbac and E. Toth in eds.:, The Chemistry of Contrast Agent in Medical Resonance Imaging, Wiley, New York (2001).
8. F. Rosch and E. Forsell-Aronsson, *Met. Ions. Biol. Syst.*, **42**, 77 (2004).
9. W.F. Finn and M.S. Joy, *Curr. Med. Res. Opin.*, **21**, 657 (2005).
10. J. Mendham, R.C. Denney, J.D. Baranes and M. Thomas, Vogel's Textbook of Quantitative Chemical Analysis, Pearson Education, edn. 6 (2004).
11. M. Valcarcel, Principles of Analytical Chemistry: A Textbook, Springer (2008).
12. R.P. Mathur and A. Arora, *Orient. J. Chem.*, **17**, 209 (2001).

13. A. Sharma, A. Arora, K. Mathur and R.P. Mathur, *Orient. J. Chem.*, 19 (2003).
14. K.G. Sharma, R.S. Shekhacoat and R.K. Mehta, *Indian J. Chem.*, **19A**, 1025 (1980).
15. J. Bartis, M. Damkova, J.J. Lessmann, L.Q. Hi, W.D. Horrochs and L.C. Francescoxi, *Inorg. Chem.*, **38**, 1042 (1999).
16. Q.-B. Song, G.-R. Qiang, T.-H. Shen, Z.-P. Yung, Y.-M. Liang, X.-L. Wu and Y.-X. Ma, *Synth. React. Inorg. Metal Org. Nano Met. Chem.*, **34**, 479 (2005).
17. X. Xu, M. Ma, Y.M. Yao, Y. Zhang and Q. Shen, *J. Mol. Struc.*, **743**, 163 (2005).
18. B.R. Judd, *Phys. Rev.*, **127**, 750 (1962).
19. G.S. Ofelt, *J. Chem. Phys.*, **37**, 511 (1962).
20. W.T. Carnall, P.R. Fields and K. Rajnak, *J. Chem. Phys.*, **49**, 4424 (1968).
21. A.H. Quati and A.G.M. Sehemi, *J. KAU Sci.*, **7**, 57 (1995).
22. S.P. Tandon and P.C. Mehta, *J. Chem. Phys.*, **52**, 4896 (1969).
23. S.P. Tandon and P.C. Mehta, *J. Chem. Phys.*, **52**, 5417 (1969).
24. B.G. Wybourne, *J. Chem. Phys.*, **36**, 2301 (1962).
25. B.G. Wybourne, *J. Chem. Phys.*, **36**, 2295 (1961).
26. C.K. Jorgenson, R. Papalardo and H.H. Schmidth, *J. Chem. Phys.*, **39**, 1422 (1963).
27. S.P. Sinha, *Spectrochim. Acta*, **22**, 57 (1966).
28. C.K. Jorgenson, Absorption Spectra and Chemical Bonding in Complexes, Pergamon Press, Oxford (1962).
29. S.Z. Misumi, S. Kida, T. Isobe and A. Inazumi, *Bull. Chem. Soc. (Japan)*, **41**, 25 (1968).
30. Th.D. Singh, C.H. Sumitra, N.I. Devi and N.R. Singh, *J. Chem. Sci.*, **116**, 303 (2004).
31. S.N. Mishra and S.D. Sommerer, *Appl. Spec. Rev.*, **26**, 151 (1991).
32. S.P. Tandon, R. Bhargawa and B. Bhatia, *Indian J. Phys.*, **65**, 180 (1991).
33. D. Hughes, M. Dane, A. Ernst, W. Hergert, M. Luders, J. Poulter, J.B. Staunton, A. Svane, Z. Szotek and W.M. Temmerman, *Nature*, **446**, 650 (2007).