GREENER APPROACH TO STUDY PHYSICOCHEMICAL PARAMETERS OF DYSPROSIUM (III) COMPLEXES WITH SOME HYPOGLYCEMIC SULFONYLUREA COMPOUNDS

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ABSTRACT

Absorption studies of Dy (III)-complexes with Hypoglycemic sulfonylurea compounds as Glimepiride, Glibenclamide and Gliclazide have been done in UV-Visible spectral range from 350 nm to 800 nm. In the optical absorption spectra, four electronic absorption bands viz $(^4P,^4D)_{3/2}$, $^4F_{7/2}$, $^4G_{11/2}$,$^6F_{3/2}$ were selected to study physicochemical parameters. Twelve systems have been investigated as doped system in different medium as non-micellar (DMF) and micellar medium (HTAB, SDS and TWEEN 80). Oscillator strength is main focus of evaluation of parameters as it is found very sensitive to some transitions known as hypersensitive transitions. Micellar effect plays a key role in enhancement of the intensity of hypersensitive electronic transition. In the micellar medium the various physicochemical parameters viz: oscillator strength, Judd Ofelt parameter and covalency parameters were observed divergent as comparative to conventional solvent systems.

KEYWORDS: Hypoglycemic sulfonylurea compounds, Oscillator Strength, Judd Ofelt Parameters, Micellar Medium, Covalency Parameters,

1. INTRODUCTION

Micellar solvent systems are advantageous over conventional solvents as these provide better platform to the interacting species by the solubilization phenomenon. Micellar systems are found to enhance various activities of interacting species at molecular level. Use of micellar surfactant systems in domestic fields for washing and clothing, now a days are turned in their interesting new fields of researches, as these are safer, environment friendly and follows the principles of green chemistry [1-4].

Lanthanides are generally found as oxides and fluorides in rocks, ores and minerals. Lanthanides are found in earth's crust in very small amount, therefore these elements are known as rare earth elements. Lanthanides are highly suitable for cellular application in the appearance of biological reducing agents, such as thiols and ascorbate, because of the redox stability of Ln^{3+} ions [5-6]. Complexes of the gadolinium like gadopentetic acid and gadoteric acid are often used as MRI contrast agents for cancer imaging, because Gd^{3+}

ion have high magnetic moment (due to presence of seven unpaired 4f electrons) and long electronic relaxation time [7-8]. Lanthanides have binding factors like high coordination number and lability in substitution to coordinate with the biomolecules. Therapeutic radioisotope applications of the lanthanides are also the field of interest for researchers. Lanthanides as agents have wide range of pharmacological applications in radio-immunotherapy and photodynamic therapy [9-12].

The activity or toxicity of Ln^{3+} (non-essential metal ion) can be decided by the deviation from reference essential metal ion like Ca^{2+} ion, mainly in redox tendency, softness and covalency. In above aspects lanthanide ion are very close to the Ca^{2+}ion, so the alteration in charge, radii and 4f orbital involvement of lanthanide ion can develop the minor adverse effect which can be controlled by the effective concentration of Ln^{3+} ion [13]. Coordination properties of rare earth ions are almost equivalent because of their similar charge, size and orbitals, but the different metal center in complexes can affect the excited state life time, luminescence intensity and emission wave length [14-16]. Ladder like electronic structure of Ln^{3+} ions, crystal field effect, deeply buried 4f electrons which are shielded by 5s and 5p, like factors originate these specific features [17-18].

Lanthanide based functional materials have some specific absorption characteristics, due to this reason these are the center of attraction for scientists and engineers in luminescence studies, Raman spectroscopy, bio-imaging and industrial applications. Rare earth ion-based systems have unique spectroscopic properties like narrow absorption or emission bands and long luminescence life time [19-21]. Lanthanide complexes plays an important role in cancer diagnosis due to the multifaceted chemical and magnetic properties of lanthanide metal ion [22]. Lanthanide have importance in medical diagnosis as an anticancer material and as an outstanding diagnostic prognostic probe [23]. Gd(III) have been used as contrast enhancing agents in Magnetic resonance imaging (MRI), because of its high spin paramagnetism and long electron relaxation times [24-25].

Dysprosium has a wide range of its application in different fields. In permanent magnets dysprosium is specially used to maintain the magnetic strength at intense heat. Recently permanent magnet is used in MRI machines and in industrial air conditioner because they can reduce 50% power consumption as compared to conventional air conditioner technology. Electric vehicles and direct drive wind turbines, dysprosium doped permanent magnets are ideally used. Due to the deficiency in fossil fuels and gradual increase in fuel prices, the technologies like electric cars and direct drive wind mills can be used in future because they make energy supply more sustainable [26-28]. Dysprosium ion play an important role for mid infrared laser development, because of its unique spectroscopic properties [29]. Complexes of Dy(III) which have very short electronic relaxation times are very useful as NMR shift reagents [30]. Many drugs in form of metallic complexes, reveal modified pharmacological properties. It has been found from the literature that metal complexes are more biologically active and less toxic as compared to the free ligand [31].

In this investigation of metal ligand complexes, Hypoglycemic sulfonylurea compounds used as ligands and Dysprosium(III) used as metal ion. Hypoglycemic sulfonylurea compounds are used in the treatment of type-2 diabetes mellitus, because these compounds act as anti-diabetic drugs [32-33]. There are two generations of sulfonylurea compounds. Tolbutamide and chlorpropamide, which are no longer in use are related to first generation. Glimperide (GPR), Glibenclamide (GBC) and Gliclazide (GCZ) are related to second generation sulfonylurea. Second generation sulfonylurea are used in the treatment of type-2 diabetes [34-36].

Objectives of present spectral absorption study are to know about the different physiochemical parameters, hypersensitive peak, environment of metal-ligand coordination sphere, interaction of metal-ligand as covalency parameters and consequences of greener micellar solvent systems on hypersensitivity and other parameters for Dysprosium(III) with Glimepiride, Glibenclamide and Gliclazide hypoglycemic sulfonylurea compounds in spectral range 350 nm to 800 nm in different conventional solvent and micellar medium.

2. EXPERIMENTATION

2.1 Preparation of Solutions

Hypoglycemic sulfonylurea compounds Glimepiride (GPR), Glibenclamide (GBC) and Gliclazide (GCZ) are purchased from life care neuro products Ltd., Dharampur, Solan. Dy(III) chloride purchased from Byahut scientico, Jaipur, manufactured by central drug house (P) Ltd. Dimethylformamide (DMF), anionic surfactant Sodium dodecyl sulfate (SDS), cationic surfactant Cetyltrimethylammonium bromide (HTAB) and non-ionic surfactant Polyethylene glycol sorbitan monooleate (Tween 80), purchased from Loba chemia Pvt. Ltd., Mumbai, India. Analytical grade of pure chemicals was used during the entire experiment.

2.2 Parameters

2.2.1 Oscillator Strength: - The measurement of intensity of an absorption band done by Oscillator strength 'P' which is a dimensionless quantity [37-38]. Oscillator Strength (P_{obs}) can be calculated by the Equation 1, showing relationship with half band width of an absorption band($\Delta V^{1/2}$) as well as with molar absorptivity (ε_{max}).

$$P_{obs} = 4.6\times 10^{-9} \times \varepsilon_{max} \times \Delta V^{1/2} \text{----------(1)}$$

where

$$\varepsilon_{max} = OD/C \times L \text{----------(2)}$$

C= Concentration of solution, OD= Optical density of sample, L= Path length of solution

2.2.2 Judd Ofelt Parameters: -For the calculation of oscillator strength of the lanthanide f→f electronic transitions a model has been proposed by Judd and Ofelt [39-40]. Judd Ofelt Parameters (T_λ) i.e., T_2 T_4 and T_6 (T_λ) are calculated by equation (3).

$$P = T_2\bar{\upsilon}\ [U^{(2)}]^2 + T_4\bar{\upsilon}\ [U^{(4)}]^2 + T_6\bar{\upsilon}\ [U^{(6)}]^2 \text{----------(3)}$$

$U^{(2)}, U^{(4)}, U^{(6)}$ = Matrix elements, $\bar{\upsilon}$ = energy of transition

2.2.3 Covalency Parameters: -Parameters used as support for covalency existence can be calculated as shown in equation (4-7).

a) $\boldsymbol{\beta}$**:** -Nephelauxetic ratio

$$\boldsymbol{\beta} = \frac{\text{average bond position in absorption spectra of the complex in wavenumber}}{\text{average bond position in absorption spectra of free ion in wavenumber}} \text{----------(4)}$$

b) $\boldsymbol{b^{\frac{1}{2}}}$ **:** − bonding parameterare calculated by equation (5) showing relationship with Nephelauxetic ratio

$$b^{\frac{1}{2}} = [\ \tfrac{1}{2}\ (1-\beta)]^{\frac{1}{2}} \text{----------(5)}$$

c) $\boldsymbol{\delta}$ **:** −S.P. Sinha introduce δ scale as.

$$\delta = \frac{(1-\beta)}{\beta} \times 100 \text{----------(6)}$$

d) $\boldsymbol{\eta}$ **:** − Covalency angular overlap parameter given as

$$\eta = \frac{(1-\beta)^{1/2}}{\beta^{1/2}} \text{----------(7)}$$

3. RESULT AND DISCUSSION

Electronic spectra of the (metal: ligand) 1:3 ratio was recorded on double beam UV-Visible spectrophotometer in the spectral range 350 to 800 nm. For the study of Dy(III) ion and GPR, GBC and GCZ doped systems electronic spectrum obtained in the non-micellar medium (DMF) and micellar medium (HTAB, SDS, TWEEN 80). Four bands ($^4P,^4D)_{3/2}$, $^4F_{7/2}$, $^4G_{11/2}$,$^6F_{3/2}$ have been observed in the optical absorption spectra of the Dy(III)-complexes [Dy(III)-GPR, Dy(III)-GBC and Dy(III)-GCZ]. For the absorption band $(^4P,^4D)_{3/2}$, highest oscillator strength P_{exp} are found in the micellar medium HTAB for Dy(III)-GPR and Dy(III)-GCZ complexes whereas for Dy(III)-GBC complex highest P_{exp} oscillator strength are found in SDS medium. Absorption band $^4F_{7/2}$ have highest oscillator strength in the micellar medium HTAB in all the doped systems Dy(III)-GPR, Dy(III)-GBC and Dy(III)-GCZ. For complexes Dy(III)-GPR and Dy(III)-GBC absorption band $^4G_{11/2}$ have highest oscillator strength in SDS micellar medium whereas for Dy(III)-GCZ complex highest P_{exp} oscillator strength for absorption band $^4G_{11/2}$ found in micellar medium HTAB. For the absorption band $^6F_{3/2}$ highest oscillator strength have been found in the micellar medium HTAB for Dy(III)-GPR and Dy(III)-GCZ complexes while for Dy(III)-GBC complex highest value are found in SDS medium (Table-1).

On comparing electronic spectra and P_{exp} oscillator strength values among all these absorption band, $^4F_{7/2}$ band have highest oscillator strength specially in micellar greener medium HTAB. So $^6H_{15/2} \rightarrow ^4F_{7/2}$ electronic transition is called 'hypersensitive transition', because this electronic transition has greater alteration in the oscillator strength than other termed as non-hypersensitive transitions. On comparing absorption spectra, magnitude of ε_{max} and their outcome values of P_{exp} oscillator strength (Table-1),$^6H_{15/2} \rightarrow ^4F_{7/2}$ transition have highest magnitude of oscillator strength in Dy(III)-GPR, Dy(III)-GBC, Dy(III)-GCZ complexes in micellar medium. Lanthanide metal complexes consists some covalent characters with the ionic bond. The T_2 parameter is influenced by the covalent bonding. Increase in the value of T_2 is attributed to the more covalency in M-L bond, because T_2 is closely related to the hypersensitive transitions. hypersensitivity, which is related to the covalency parameter in term of nephelauxetic ratio (β) characterized in Table 2-3. For the complexes Dy(III)-GPR, Dy(III)-GCZ value of T_2 parameter are found highest in HTAB micellar medium but for Dy(III)-GBC complex highest value of T_2 are found in SDS micellar medium.

Refractive index of the medium T_4 and Judd Ofelt parameterT_6, which is the indicative of the degree of the change in symmetry around the metal ion, due to ligand environment, were found highest in the micellar medium HTAB for the Dy(III)-GPR and Dy(III)-GCZ complexes, whereas for the Dy(III)-GBC complex highest value of T_4 and T_6 is found in the micellar greener medium SDS. Constant value of the coordination parameter T_4/T_2 ratio, indicate that metal ion Dy(III) have same coordination environment around it. The value of T_4/T_6 ratio varies from 0.25 to 0.55, which depicted the variation in the symmetry around the doped Dy(III) ion in saturated ligand solution Table-2.

Nephelauxetic ratio (β), S.P. Sinha's covalency parameter 'δ scale' and covalency angular overlap parameter, bonding parameter ($b^{1/2}$), which are the covalency parameters are represented in the Table-3. For Dy(III)-GCZ complex, the lowest in value and more significant nephelauxetic ratio (β) have been observed in HTAB surfactant medium among all three doped complex systems Dy(III)-GPR, Dy(III)-GBC and Dy(III)-GCZ in DMF and micellar HTAB, SDS and TWEEN 80 medium. The value of nephelauxetic ratio is less than one, which shows the shifting of absorption bands towards higher wavelength for Dy(III)-complexes as compared to the free metal ion Dy(III). Shifting of absorption bands are found highest in DY(III)-GCZ in HTAB micellar medium. β value far from unity inferred more covalency characters in the metal-ligand complexes.

The value of bonding parameter $b^{1/2}$ have been found highest in HTAB micellar medium for ligand GCZ on complexation with Dysprosium metal ion among all 12 doped systems. Highest δ scale' Sinha's covalency parameter are also found high for DY(III)-GCZ in HTAB which shows highest covalency character in the

present study of Dy(III)-GPR, Dy(III)-GBC and Dy(III)-GCZ metal-ligand complexes.

Table-1

DY(III)-Complexes with Hypoglycemic Sulfonylurea compounds in non-micellar medium [DMF] and Micellar medium [HTAB, SDS and TWEEN 80] with the value of calculated Oscillator Strength.

S. No.	LEVEL	$(^4P, ^4D)_{3/2}$		$^4F_{7/2}$		$^4G_{11/2}$		$^6F_{3/2}$		r.m.s dev. $\pm\sigma$ x 10^6
	DOPED SYSTEMS	P_{exp}	P_{cal}	P_{exp}	P_{cal}	P_{exp}	P_{cal}	P_{exp}	P_{cal}	
1	DY(III)-GPR (DMF)	14.75	31.04	10.72	25.98	13.47	27.39	3.13	10.97	13.72
2	DY(III)-GPR (HTAB)	30.49	72.81	39.85	79.75	10.51	46.63	5.37	4.97	35.71
3	DY(III)-GPR (SDS)	21.32	41.28	26.99	45.86	14.75	31.79	4.97	14.57	16.86
4	DY(III)-GPR (TWEEN)	13.24	21.90	14.90	23.07	13.27	20.67	3.56	7.73	7.31
5	DY(III)-GBC (DMF)	14.90	31.51	18.28	33.95	13.22	27.41	3.141	11.12	14.02
6	DY(III)-GBC (HTAB)	13.09	19.15	35.14	40.89	11.89	17.08	3.85	4.88	5.12
7	DY(III)-GBC (SDS)	34.19	90.45	27.84	80.96	13.60	61.56	4.88	31.90	47.47
8	DY(III)-GBC (TWEEN)	13.19	21.84	31.84	40.06	10.80	18.24	3.58	7.76	7.33
9	DY(III)-GCZ (DMF)	13.26	24.72	19.47	30.30	8.82	18.63	3.22	8.73	9.68
10	DY(III)-GCZ (HTAB)	24.69	39.51	110.83	124.83	21.69	34.42	6.86	3.81	12.53
11	DY(III)-GCZ (SDS)	13.05	19.34	18.89	24.86	13.44	18.84	3.81	6.84	5.32
12	DY(III)-GCZ (TWEEN)	17.75	36.16	38.80	56.24	14.11	29.86	3.92	12.79	15.56

Table-2

DY(III)-Complexes with Hypoglycemic sulfonylurea compounds in non-micellar medium [DMF] and Micellar medium [HTAB, SDS and TWEEN 80] with the value of calculated T_λ Parameters

S. NO.	DOPED SYSTEMS	T_2x10^{10}	T_4x10^{10}	T_6x10^{10}	T_4/T_2	T_4/T_6
1	DY(III)-GPR (DMF)	21952.27	88.69	185.74	0.0040	0.47
2	DY(III)-GPR (HTAB)	72759.85	110.29	435.10	0.0015	0.25
3	DY(III)-GPR (SDS)	40621.89	92.20	246.37	0.0022	0.37
4	DY(III)-GPR(TWEEN)	19657.01	69.97	130.89	0.0035	0.53
5	DY(III)-GBC (DMF)	29481.78	87.78	188.29	0.0029	0.46
6	DY(III)-GBC (HTAB)	37219.96	55.62	114.61	0.0014	0.48
7	DY(III)-GBC (SDS)	71918.84	157.42	539.79	0.0021	0.29
8	DY(III)-GBC (TWEEN)	36521.84	56.29	131.41	0.0015	0.42
9	DY(III)-GCZ (DMF)	27216.72	52.76	147.76	0.0019	0.35
10	DY(III)-GCZ (HTAB)	116774.38	109.92	237.17	0.0009	0.46
11	DY(III)-GCZ (SDS)	21491.67	64.82	115.88	0.0030	0.55
12	DY(III)-GCZ (TWEEN)	50649.09	91.74	216.36	0.0018	0.42

Table-3

DY(III)-Complexes with Hypoglycemic Sulfonylurea Compounds non-micellar medium [DMF] and Micellar medium [HTAB, SDS and TWEEN 80] for Covalency parameter's [β, $b^{1/2}$, δ% and η] computed value.

S.No.	DOPED SYSTEMS	β	$b^{1/2}$	δ	η
1	DY(III)-GPR (DMF)	0.9943	0.0533	0.5722	0.0028
2	DY(III)-GPR (HTAB)	0.9963	0.0426	0.3645	0.0018
3	DY(III)-GPR (SDS)	0.9990	0.0215	0.0928	0.0004
4	DY(III)-GPR (TWEEN)	0.9973	0.0364	0.2659	0.0013
5	DY(III)-GBC (DMF)	0.9972	0.0369	0.2738	0.0013
6	DY(III)-GBC (HTAB)	0.9946	0.0516	0.5370	0.0026
7	DY(III)-GBC (SDS)	0.9976	0.0340	0.2318	0.0011
8	DY(III)-GBC (TWEEN)	0.9950	0.0498	0.5003	0.0024
9	DY(III)-GCZ (DMF)	0.9970	0.0381	0.2925	0.0014
10	DY(III)-GCZ (HTAB)	0.9935	0.0567	0.6476	0.0032
11	DY(III)-GCZ (SDS)	0.9977	0.0334	0.2236	0.0011
12	DY(III)-GCZ (TWEEN)	0.9964	0.0423	0.3592	0.0017

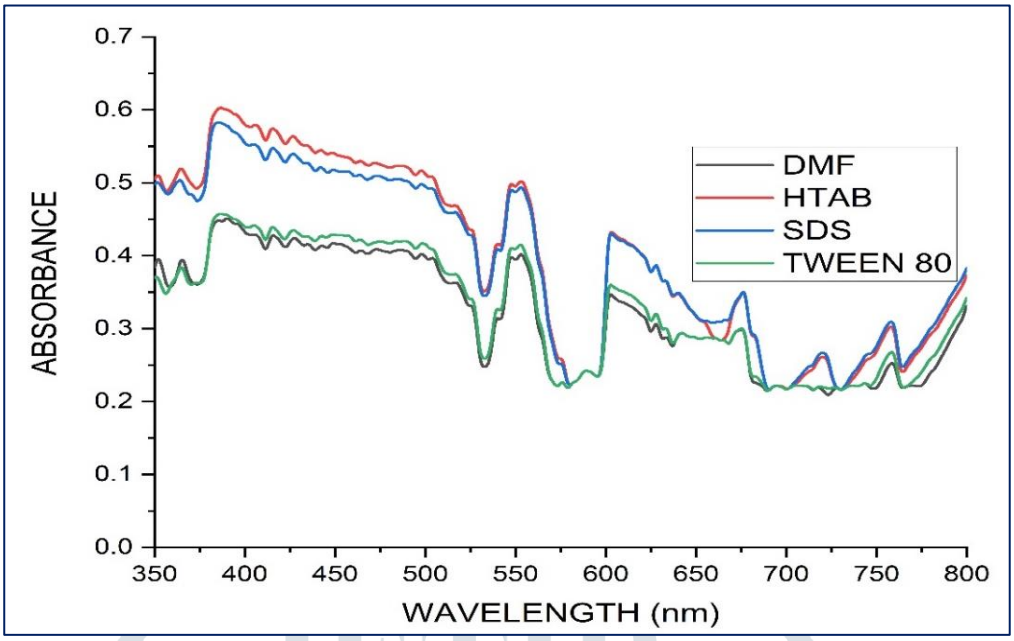

Figure: -1 Electronic spectrum of Dy(III)-GPR Complex in non-micellar medium **(**DMF) and micellar medium (HTAB, SDS and TWEEN 80).

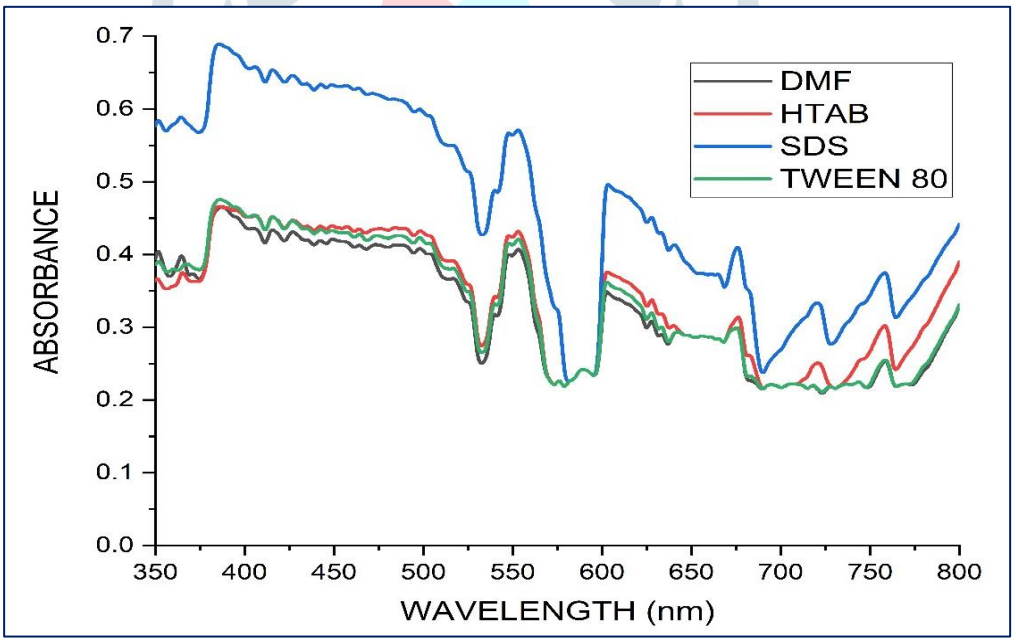

Figure: -2 Electronic spectrum of Dy (III)-GBC Complex in non-micellar medium (DMF) and micellar medium (HTAB, SDS and TWEEN 80).

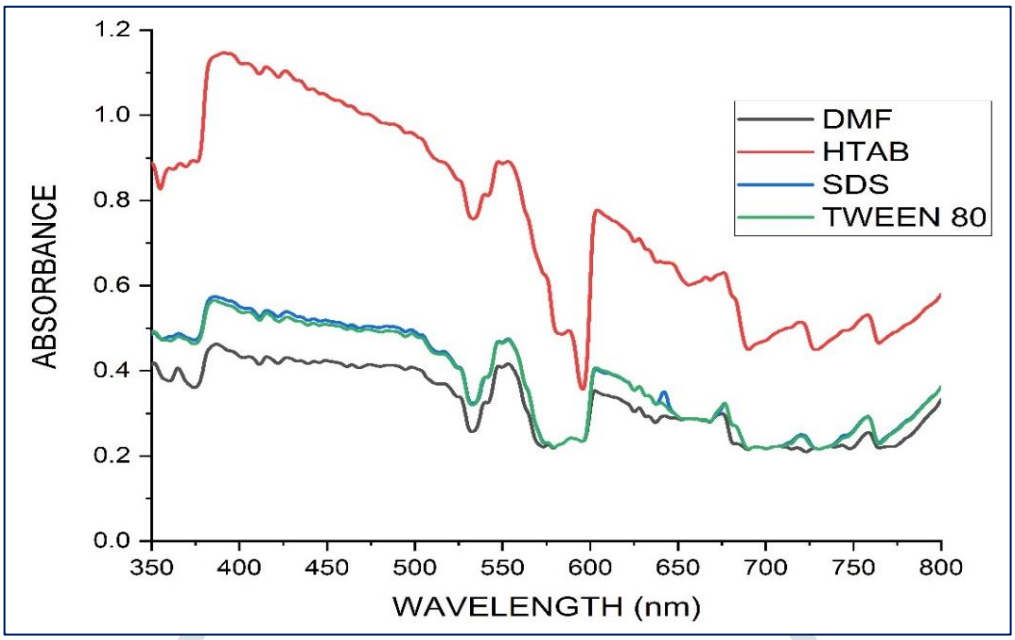

Figure: -3 Electronic spectrum of Dy (III)-GCZ Complex in non-micellar medium (DMF) and micellar medium (HTAB, SDS and TWEEN80).

4. CONCLUSION

Aqueous micellar solvent systems, a greener approach, being safer and ecofriendly, provides better contact for interacting species and proves a better solvent system than conventional solvents. The investigations on the doped systems, Dy(III) ion as metal ion and hypoglycemic sulfonylurea compounds Glimperide, Glibenclamide and Gliclazide as ligands in micellar medium (HTAB, SDS and TWEEN 80) have greater magnitude of parameters exploited from spectral study comparative to conventional solvent DMF. Various spectral parameters Oscillator strength(P) and Judd-Ofelt parameters (T_λ=T_2, T_4, T_6) have been exploited from spectral studies and inferred that in micellar medium interaction between metal ion and ligands takes place to somewhat greater extent resulting change in the shape and shifting of the absorption bands.

Presence of covalency is depicted in metal-ligand systems, through different parameters, are the key factor of this absorption spectral study. Sensational changes are occurring in different spectral parameter in greener micellar systems, indicating the interaction of f-orbital of the metal ion with ligands and spin-orbit interaction occurs which generate the f→f transition. The changes in bonding parameters like β, δ, $b^{1/2}$, η and oscillator strength (P) indicate, the interaction of the f-orbital of Dy(III) with the ligands Glimepiride (GPR), Glibenclamide (GBC) and Gliclazide (GCZ) present in the greener saturated solution.

The small root mean square deviation, which varies from 5.12×10^{-6} to 47.4×10^{-6}, propose the validity of Judd-Ofelt theory of f→f transition (Table-1). From the electronic spectrum of the doped system Dy(III)-GPR, Dy(III)-GBC and Dy(III)-GCZ, red shift has been observed for all electronic transition bands as compare to the free metal ion, indicating the metal-ligand interaction and shifting of electron density towards the Glimperide, Glibenclamide and Gliclazide ligands Figure 1-3. and Table 1-3. As being hypersensitive $^6H_{15/2} \rightarrow {}^4F_{7/2}$ transition, have highest oscillator strength than other three absorption bands in absorption spectra. Micellar greener solvent HTAB shows a peculiar change in different parameters for Dy(III)-Gliclazide, metal-ligand complex.

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6. REFERENCES

(1) Pharr, D.Y. 2017. Green analytical chemistry–the use of surfactants as a replacement of organic solvents in spectroscopy. *Physical Sciences Reviews*, *2*(7): 1-25

(2) Paprocki, D., Madej, A., Koszelewski, D., Brodzka, A. and Ostaszewski, R. 2018. Multicomponent reactions accelerated by aqueous micelles. *Frontiers in Chemistry*, *6*:1-21.

(3) Schott, H. 1985. Surfactant systems: Their chemistry, pharmacy and biology. By D. Attwood and AT Florence. Chapman & Hall, London EC4P 4EE, United Kingdom. 1983. 794.

(4) Jee, R.D. 1995. Study of micellar solutions to enhance the europium-sensitized luminescence of tetracyclines. *Analyst*, *120*(12): 2867-2872.

(5) Beatty, R. 2008. *The Lanthanides*. Marshall Cavendish Benchmark.

(6) Buenzli, J.C.G. 2015. On the design of highly luminescent lanthanide complexes. *Coordination Chemistry Reviews*, *293*: 19-47.

(7) Ghiassi, K.B., Olmstead, M.M. and Balch, A.L.2014. Gadolinium-containing endohedral fullerenes: structures and function as magnetic resonance imaging (MRI) agents. *Dalton Transactions*, *43*(20): 7346-7358.

(8) Teo, R.D., Termini, J. and Gray, H.B. 2016. Lanthanides: Applications in cancer diagnosis and therapy: miniperspective. *Journal of medicinal chemistry*, *59*(13): 6012-6024.

(9) Kostova, I., 2005. Lanthanides as anticancer agents. *Current Medicinal Chemistry-Anti-Cancer Agents*, *5*(6): 591-602.

(10) Gao, E., Ding, Y., Sun, N., Zhang, S., Qiu, X., Zhan, Y. and Zhu, M. 2017. Synthesis, characterization, DNA interaction, apoptosis and molecular docking of Cu (II) and Mn (II) complexes with endo-norbornene-cis-5, 6-dicarboxylic acid. *Applied Organometallic Chemistry*, *31*(3): 3575(1-8).

(11) Gao, E., Qi, Z., Qu, Y., Ding, Y., Zhan, Y., Sun, N., Zhang, S., Qiu, X. and Zhu, M. 2017. Two novel dinuclear ellipsoid Ni (II) and Co (II) complexes bridged by 4, 5-bis (pyrazol-1-yl) phthalic acid: Synthesis, structural characterization and biological evaluation. *European Journal of Medicinal Chemistry*, *136*: 235-245.

(12) Purim, O., Beny, A., Inbar, M., Shulman, K., Brenner, B., Dudnik, E., Bokstein, F., Temper, M., Limon, D., Matceyevsky, D. and Sarid, D. 2018. Biomarker-driven therapy in metastatic gastric and esophageal cancer: real-life clinical experience. *Targeted Oncology*, *13*(2): 217-226. Wang, K., Li, R., Cheng, Y. and Zhu, B. 1999. Lanthanides—the future drugs?. *Coordination Chemistry Reviews*, *190:* 297-308.

(13) Wang, K., Li, R., Cheng, Y. and Zhu, B. 1999. Lanthanides—the future drugs?. *Coordination Chemistry Reviews*, *190:* 297-308.

(14) Li, H., Xie, C., Lan, R., Zha, S., Chan, C.F., Wong, W.Y., Ho, K.L., Chan, B.D., Luo, Y., Zhang, J.X. and Law, G.L. 2017. A Smart Europium–Ruthenium complex as anticancer prodrug: Controllable drug release and real-time monitoring under different light excitations. *Journal of medicinal chemistry*, *60*(21): 8923-8932.

(15) Liu, D., Zhou, Y.N., Zhao, J., Xu, Y., Shen, J. and Wu, M. 2017. An intensive green emitting terbium complex using a newly designed aromatic hyperbranched polyester as an efficient antenna ligand. *Journal of Materials Chemistry*, *5*(44): 11620-11630.

(16) Zhang, T., Zhu, X., Cheng, C.C., Kwok, W.M., Tam, H.L., Hao, J., Kwong, D.W., Wong, W.K. and Wong, K.L. 2011. Water-soluble mitochondria-specific ytterbium complex with impressive NIR emission. *Journal of the American Chemical Society*, *133*(50): 20120-20122.

(17) Malta, O.L. 2008. Mechanisms of non-radiative energy transfer involving lanthanide ions revisited. *Journal of non-crystalline solids*, *354*(42-44): 4770-4776.

(18) Wybourne, B.G. and Smentek, L. 2007. *Optical spectroscopy of lanthanides: magnetic and hyperfine interactions*. CRC press.

(19) Sastri, V.S., Perumareddi, J.R., Rao, V.R., Rayudu, G.V.S. and Bunzli, J.C., 2003. *Modern aspects of rare earths and their complexes*. Elsevier.

(20) Runowski, M., Marciniak, J., Grzyb, T., Przybylska, D., Shyichuk, A., Barszcz, B., Katrusiak, A. and Lis, S. 2017. Lifetime nanomanometry–high-pressure luminescence of up-converting lanthanide nanocrystals–SrF 2: Yb 3+, Er 3+. *Nanoscale*, *9*(41): 16030-16037.

(21) Binnemans, K., 2009. Lanthanide-based luminescent hybrid materials. *Chemical reviews*, *109*(9): 4283-4374.

(22) Teo, R.D., Termini, J. and Gray, H.B., 2016. Lanthanides: Applications in cancer diagnosis and therapy: miniperspective. *Journal of medicinal chemistry*, *59*(13): 6012-6024.

(23) Misra, S.N., Gagnani, M.A. and Shukla, R.S., 2004. Biological and clinical aspects of lanthanide coordination compounds. *Bioinorganic Chemistry and Applications*, *2*(3-4): 155-192.

(24) Caravan, P., Ellison, J.J., McMurry, T.J. and Lauffer, R.B., 1999. Gadolinium (III) chelates as MRI contrast agents: structure, dynamics, and applications. *Chemical reviews*, *99*(9): 2293-2352.

(25) Toth, E., Helm, L. and Merbach, A.E., 2001. Relaxivity of gadolinium (III) complexes: theory and mechanism. *The chemistry of contrast agents in medical magnetic resonance imaging*, *2*.

(26) Hoenderdaal, S., Espinoza, L.T., Marscheider-Weidemann, F. and Graus, W. 2013. Can a dysprosium shortage threaten green energy technologies? *Energy*, *49:* 344-355.

(27) McGill, I. 2000. Rare earth elements. *Ullmann's encyclopedia of industrial chemistry*.

(28) Lusty, P. and Walters, A. 2010. Rare earth elements. *British Geological Survey*.

(29) Majewski, M.R., Woodward, R.I. and Jackson, S.D. 2018. Dysprosium-doped ZBLAN fiber laser tunable from 2.8 μm to 3.4 μm, pumped at 1.7 μm. *Optics letters*, *43*(5): 971-974.

(30) Peters, J.A., Huskens, J. and Raber, D.J., 1996. Prog. AM in ref. 15b, 99; Chen, D.; Motekaitis, RJ. *Nucl. Magn. Reson. Spectrosc*, *28:* 283.

(31) El-Houte, S. and El-Sayed Ali, M., 1991. Thermal decomposition of cerium oxalate and mixed cerium-gadolinium oxalates. *Journal of thermalanalysis*, *37*(5): 907-913.

(32) Derosa, G. and Maffioli, P., 2011. Thiazolidinediones plus metformin association on body weight in patients with type 2 diabetes. *Diabetes Research and Clinical Practice*, *91*(3): 265-270.

(33) Derosa, G., Tinelli, C. and Maffioli, P., 2009. Effects of pioglitazone and rosiglitazone combined with metformin on body weight in people with diabetes. *Diabetes, Obesity and Metabolism*, *11*(12): 1091-1099.

(34) Tessier, D., Dawson, K., Tetrault, J.P., Bravo, G. and Meneilly, G.S., 1994. Glibenclamide vs gliclazide in type 2 diabetes of the elderly. *Diabetic medicine*, *11*(10): 974-980.

(35) Pfeifer, M.A., Halter, J.B., Graf, R. and Porte Jr, D., 1980. Potentiation of insulin secretion to nonglucose stimuli in normal man by tolbutamide. *Diabetes*, *29*(5): 335-340.

(36) Ballagi-Pordány, G., Köszeghy, A., Koltai, M.Z., Aranyi, Z. and Pogátsa, G., 1990. Divergent cardiac effects of the first- and second-generation hypoglycemic sulfonylurea compounds. *Diabetes research and clinical practice*, *8*(2): 109-114.

(37) Carnall, W.T., Fields, P.R. and Wybourne, B.G., 1965. Spectral intensities of the trivalent lanthanides and actinides in solution, I. Pr^{3+}, Nd^{3+}, Er^{3+}, Tm^{3+}, and Yb^{3+}. *J. Chem. Phys.*, *42*(11), pp.3797-3806.

(38) Carnall, W.T. and Fields, P.R., Rajnak K 1968. *J. Chem. Phys*, *49*: 442
(39) Judd, B.R., 1962. Optical absorption intensities of rare-earth ions. *Physical review*, *127*(3): 750.
(40) Ofelt, G.S., 1962. Intensities of crystal spectra of rare-earth ions. *The journal of chemical physics*, *37*(3): 511-520.