

**EVALUATION OF EUROPIUM DOPED GADOLINIUM OXIDE
AND ORTHOVANADATE NANOSYSTEMS AND THEIR
BIOPHYSICAL RELEVANCE**

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By

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Chapter VIII
Conclusions and future directions

There has been significant progress made in recent time in the quest for suitable, efficient and affordable nanophosphors. Incidentally, matchless scope in a wide and diverse range of applications of the rare-earth (RE) oxides and vanadate based nanosystems has been visualized. The nanosystems display excellent optical, optoelectronic properties and consequently, they find applications in various domains *viz.* as low threshold lasers, high performance luminescent panels, frequency up-converters, photocatalytic agents, drug-carriers, magnetic resonance imaging (MRI) contrast agent, biosensing and biolabelling applications.

Gadolinium oxide (Gd_2O_3) and gadolinium vanadate (GdVO_4) act as important hosts which can accommodate suitable dopants (especially transition metals, alkali or RE ions) to yield nanophosphors of certain kind turning it to be extremely popular in processing efficient nanophosphors [1-6]. More precisely, incorporation of selectively chosen RE dopant and intentionally introduced defect states/trap centres via radiation exposure can influence the characteristic $5d-4f$ transitions to great extent [7, 8]. Inclusion of lanthanide ions, such as Eu^{3+} with $5d \rightarrow 4f$, or $4f \rightarrow 4f$ transitions acting as emission centres [9], along with the presence of trap centres such as lattice/intrinsic defects (e.g., oxygen vacancies, *F*-centres etc.) in the host matrix has proven to augment the bright and delayed emission responses [10, 11]. Use of co-dopants by incorporating non-RE dopant can also prove to be a vital tool in order to achieve enhanced luminescence, especially in case of nanophosphors [12]. GdVO_4 is of special interest from the optical window point of view since the excitation of the doping Ln^{3+} cation through an energy transfer mechanism from the vanadate anion is much more efficient than the direct excitation of the electronic levels of Ln^{3+} .

This thesis highlights the investigations directed towards development of a multimodal luminescent material that has high phosphorescence efficiency as well as biocompatible features. For this purpose, the host materials for Eu^{3+} activator ions are evaluated for optimal luminescence with high emission intensity profile with moderate doping and below quenching concentrations. To achieve asymmetry around the activator ions, the effect of defect creation upon γ -

irradiation and inclusion of co-dopants in the host matrix has been evaluated. An approach has been made to visualize the underlying mechanisms involved in the various processes involved. The cytotoxic effects of the nanostructures are detailed keeping in mind their potential usage in biological applications as a theranostic agent. This chapter draws conclusions from the investigations performed and observations made in the present study. The important findings are highlighted below:

- Both bottom-up and top-down approach are elucidated. Eu^{3+} doped Gd_2O_3 nanopowders (EuGNP) are prepared by citrate gel route as well as hydrothermal route doped with varying concentrations, affirming cubic phase in the X-Ray Diffraction (XRD) analysis. Meanwhile solid state mixing- cum- sintering led Eu^{3+} doped orthovanadate (EuGdV) nanosystem displayed zircon type tetragonal crystal structure. Occurrence of no extra peak suggests that unwanted phases (Eu_2O_3 and EuVO_4) are not formed separately during the preparation EuGNP and EuGdV nanosystems. Transmission Electron Microscopy (TEM) imaging allowed us to visualize the nanocrystalline features of both undoped and doped nanosystems. The interplanar distances measured from the lattice fringes using *ImageJ*[®] were found to be in good agreement with the XRD results.

- The optical band gap of the as-prepared nanosystems were determined from the optical absorption spectra analysis following Kubelka Munk (KM) method [13]. In the present case it was estimated as, ~ 5.5 eV and ~ 3.5 eV for Gd based oxides and vanadate systems, respectively. The band gaps and phonon absorption energies for the systems, were also predicted through Kumar's model [14].

- With the help of X-ray Photoelectron Spectroscopy (XPS) study, the valence band maximum (VBM) was determined to be ~ 8.4 eV and ~ 8.06 eV for EuGNP and EuGdV respectively. Effect of variation in doping level was not visualized for the VBM in case of EuGNP. However, in addition to peak shifting, upon 3 mol% Eu^{3+} doping, the VBM increased from ~ 1.1 (for undoped GdV) to ~ 1.5 (for doped GdV). Interestingly, the core level spectra of the nanosystems offered new and

captivating results. Upon Eu incorporation, characteristic peaks of +3 and +2 oxidation states of Eu are witnessed for the EuGNP system. This important observation of the additional signal from +2 oxidation state of Eu, is attributed to 'surface valence transition' involved in the oxide system, and detailed in the relevant sections. However, peak signalling occurrence of +2 state of Eu is not observed in case of the EuGdV system. Spin splitting can be witnessed from the Gd4d spectra and contribution of spin polarization to the profile was found to be greater in the case of doped nanosystems.

- With the aim and motive to probe and associate the electrically driven (ED) and magnetically driven (MD) transitions involved in Eu^{3+} , a thorough analysis of time resolved photoluminescence aspects has been made for both the oxide (EuGNP) and as well as vanadate (EuGdV) based nanosystems. Following the emission profiles of EuGNP in the blue-green regime, it can be established that a large number of crystal field transitions influence these levels to follow non-radiative transitions between ${}^5D_1 \rightarrow {}^5D_0$. From the excitation spectra of EuGdV nanosystems, energy transfer from $[\text{VO}_4]^{3-}$ tetrahedral ions to Eu^{3+} was found to display predominant excitation route. Concentration quenching was witnessed at a critical concentration of 3 mol% of Eu^{3+} doping in both the cases. Our analysis following Dexter's theory led to a stimulating observation wherein the quenching processes involved contributions from exchange interaction of ions [15]. Furthermore, the average critical distance between the activator ions beyond which quenching can occur was determined using Blasse's energy transfer equation and was found to be $\sim 1.36 \text{ \AA}$ and $\sim 1.84 \text{ \AA}$ for EuGNP, EuGdV nanosystems respectively. Out of the various transitions via ${}^5D_0 \rightarrow {}^7F_J$ ($J=0,1,2,3,4$) in the red and far red regime the ${}^5D_0 \rightarrow {}^7F_0$ transition, positioned at $\sim 580 \text{ nm}$ is a captivating observation confirming J -mixing due to crystal field perturbation and/or mixing of low lying charge transfer states into wavefunctions of $4f_6$ configuration.

- The PL emission profile of γ -irradiated EuGNP nanosystems further elates the effect of distorted local field leading to observable peak splitting. Point defect

formations due to 1.3 MeV γ -irradiation induced creation of closely packed non-radiative trap centres offered both neutral as well as ionized vacancies. Hence, it would indicate two possible excitation pathways to populate the 5D_0 level, one being via 5D_1 level and the other promoting ions directly into 5D_0 state. Non-radiative relaxation caused by the surface defects acting as quenchers was also observed after irradiation. The γ -irradiation induced manifested PL of EuGdV nanosystems and related phosphorescence decay dynamics are discussed in great detail. Moreover, a decrement in decay lifetime, up to ~ 1.33 times, with increasing irradiation dosage could be observed from the lifetime decay dynamics.

- Raman spectra of EuGDV led to observation of characteristic signals from active Raman modes *viz.* ν_2 modes at $\sim 380\text{ cm}^{-1}$, $\sim 880\text{ cm}^{-1}$ and ν_3 mode at $\sim 800\text{--}820\text{ cm}^{-1}$. While the modes at $\sim 380\text{ cm}^{-1}$ are ascribed to symmetric V-O stretching or O-V-O bending mode, the mode at $\sim 880\text{ cm}^{-1}$ is in general attributed to the vibrational structure (stretching internal vibration in $[\text{VO}_4]^{3-}$ anionic group. Meanwhile the ν_3 modes are an overlap of E_g and B_{1g} modes. Relaxation of E_g and B_g modes in ν_3 components upon Eu inclusion beyond critical concentration was determined. Captivatingly, partial *zircon* to *scheelite* type transition upon Eu^{3+} co-doping has been realized. The effect of structural disordering leading to the observations made upon Eu inclusion has been expounded upon in this chapter.

- A superior photocatalysis of *azo* based dyes has been speculated recognizing that the GdVO_4 nanosystem comes with an excellent capability to generate hydrogen from water. The photocatalytic performance of the as-derived nanocatalysts against azo dye- Congo Red (CR) has been highlighted considering daylight and UV illumination. The CR dye was apparently degraded up to $\sim 91.8\%$ by $3\% \text{Eu}^{3+}:\text{GdVO}_4$ nanocatalyst, possibly to other aromatic species, with convincing discoloration effect. Notably, the rate constant gets doubled from $\sim 0.034\text{ min}^{-1}$ to $\sim 0.071\text{ min}^{-1}$ upon inclusion of dopant into the host.

- A dependable approximation of erythrocyte deformability and processes involved are requisite for optimal evaluation of diagnostic features as well as therapeutic characteristics explicated. To be specific, hemocompatibility of

3% EuGdV nanosystem was proven to be better than 3% EuGNP nanosystem.. The cells fixed with glutaraldehyde after 1 h and 12 h of treatment with the nanosystems suffered damage and shape transformations as observed from high resolution SEM imaging studies. The percentage of transforming/damaged cells has increased upon incubation for 12 h with high cell viability (over ~95%) for 3% EuGdV system.

- In addition, the interaction of nanosystems with platelet poor plasma is checked. The hydrodynamic sizes of both the nanosystems is determined to be increased in blood plasma medium, possibly due to formation of protein corona around the charged nanoparticles. While the EuGNP displayed no or minimal effect in plasma recalcification time, a dose dependent pro-coagulant nature is evident for the EuGdV nanosystem. The plasma coagulation time almost halved upon treatment with 100 µg/ml of vanadate based nanosystem. The plasma-nanoparticle interaction is expounded upon in the thesis.

Future Directions

Gd based nanosystems have proven to be excellent hosts for Ln³⁺ dopants, displaying effective luminescent behaviour. This enables the nanosystems to be of great applicability as a phosphor in display screens as well as for bio-imaging purposes. In this regard, appropriate concentrations of dopants/co-dopants below concentration quenching, play an important role in augmented luminescence. In addition to the dopants displaying down-conversion properties, emission profiles of up-conversion (UC) Ln³⁺ ions can be evaluated as well. Moreover, Near Infra-red (NIR) excited up-conversion materials offer great utility as bio-imaging labels owing to better penetration depths and safe usage. UC NPs can thus be exploited in single-particle tracking (SPT) methods, providing valuable cellular information. Furthermore, simultaneous doping of both down-

conversion as well as up-conversion Ln^{3+} systems can be evaluated for white light emission based investigations.

In addition, the studies display nanoparticle size and dopant dependent phosphorescence and consequently the lanthanide resonance energy transfer (LRET) of the nanophosphors can be evaluated. At large, LRET enables to determine the involved energy transfer for a better visualization of the mechanisms involved. In addition, the persistent luminescence (PersL) properties can be investigated in the systems upon doping with suitable Ln^{3+} ions. PersL nanomaterials find a wide range of applications including in bio-imaging and bio-labeling.

In our study, GdVO_4 nanosystem displayed excellent dye degradation capability, apart from orange-red phosphorescence. The photocatalytic study can be extended further considering variations in the pH environment, dye type, dye/catalyst concentration ratio and irradiation dose/type. A better understanding of the photocatalytic processes and the operative conditions could offer great opportunities for its commercial benefits and industrial relevances.

In the past few decades, attention from Gd-based chelates has been shifted to Gd based nanoparticles, as regards MRI positive contrast agent. In addition to its promising usage as MRI contrast agents, gadolinium based nanoparticles also offer exciting intrinsic therapeutic properties under irradiation or applied magnetic field (hyperthermia). To be mentioned, neutron capture therapy is also applicable for cancer treatment using Gd based NPs. In this context, the γ -irradiation mediated augmentation of emission profiles of Eu^{3+} doped Gd oxides can play a major role in combining imaging and therapeutic modalities at large. Multifunctional nanosystems exhibiting both diagnostic as well as therapeutic features fall under a new category of nanomaterials, namely 'theranostic agents'.

It is noteworthy that the greatest challenge in development of a nanomaterial for clinical application is its size dependent toxicity and

agglomerative properties. Hence, evaluation of bio-viability, both *in vitro* and *in vivo* in a meticulous manner is a requisite for exploiting a nanosystem for routine application in hospitals and diagnostic centres. Assessment of effect of morphology of a nanostructures is thus vital. This demands a thorough examination of the nanosystem following wide range of bio-assays and toxicity determination techniques. Also, cellular uptake mechanisms in normal and cancerous/tumorous cell offer numerous possibilities to visualize theranostic features. Furthermore, investigation in order to understand effects of interaction of nanoparticle with blood plasma can be expounded upon. The activation of the coagulation cascade using NPs can be deemed important aspect for safe administration *in vivo*.

Also, considering the fact that Gd based nanosystem enter a cell through Ca channels, the relevant mechanisms in ion pumping and channelling can be elaborated. Such evaluation wherein role of nanostructures in activation of transport of ions (Na or K) through ion pumps located in cellular membrane can play vital role in comprehending essential life processes.

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