

Chapter I
Introduction

1.0 Nanosystems: An Introduction

Nanoscience is an interdisciplinary field of science which covers topics from varied research areas and acts as an intermediate theme for several subjects, including physics, chemistry, biology, engineering etc. The word 'nano' finds its origin in greek, and implies 'dwarf'. In mathematical terms, it is defined as 'billionth fraction of a meter'. The concept of a 'nanometer' was first suggested by Prof. Richard Zsigmondy, Nobel Laureate 1925 (Chemistry), to characterize particles of very small dimensions utilizing microscopes [1]. The domain of research drew attention of researchers following the classic talk by Prof. Richard Feynman on December 29, 1959, at the annual meeting of the American Physical Society, California Institute of Technology (Caltech), titled '*There's Plenty of Room at the Bottom: An Invitation to Enter a New Field of Physics*' [2]. In his talk, Feynmann carefully highlighted possibility of manipulating systems in atomic scale, by decreasing material size and atomic rearrangement in a practical way, emphasizing their economic utilities [2]. The term 'nanotechnology' is traditionally used to describe materials with a typical dimension ≤ 100 nm, and was coined first by Norio Taniguchi to describe semiconductor processes occurring in nanometric order [1]. Nanomaterials are thus composed of particles having at least one dimension in the range of 1–100 nm [3]. Nanotechnology deals with processing, separation, agglomeration, and deformation of materials by an atom. It was only in 1980s that enhancement of sophisticated instruments enabled discovery of fullerenes and carbon nanotubes that led to extravagant popularity of nanotechnology [4]. Eric Drexler of Massachusetts Institute of Technology his 1986 book titled, '*Engines of Creation: The Coming Era of Nanotechnology*' envisioned both the calibre and devastating negative consequences of nanotechnological interventions [5]. Since 2000s, industrial applications of nanosystems have overseen exponential growth. The beneficial usage of nanomaterials is very diverse, however, potential health hazards upon extensive human exposure to nanoparticles raises several concerns. Such concerns are dealt with 'Nanotoxicology' which is the study of risks in usage of nanomaterials [6].

Meticulous scrutiny of implications of the nanotechnology to safeguard its applications is required in this regard.

Recent advances in nanoscience have allowed researchers to apply new technically sound approaches in molecular and biological processes, thereby advancing underlying principles and mechanisms, in particular nano-bio-technology [7].

1.1. Rare earth based nanosystems

According to the International Union of Pure and Applied Chemistry (IUPAC) recommendations (1968), lanthanides (La) and actinide (Ac) series are classified in rare earth (RE) category. In particular the non-radioactive lanthanide elements normally exist in +3 oxidation state, and is relevant for all RE-Oxide systems (REO) and RE-Vanadate systems (REV) [8]. The spectroscopic properties of trivalent lanthanide ions are fascinating as their $[\text{Xe}] 4f_n$ electronic configuration offers numerous electronic levels, up to 3432 for Gd^{3+} [9]. Lanthanides first found their industrial application as a material in mantle for lighting purpose proposed by Carl Auer von Welsbach in late 1891 [9]. The luminescent trivalent lanthanide ions can follow processes which occur without change in spin either *i.e.* fluorescence, (Pr^{3+} , Nd^{3+} , Ho^{3+} , Er^{3+} , Yb^{3+}) or follow transitions with a change in spin *i.e.* phosphorescence (Sm^{3+} , Eu^{3+} , Gd^{3+} , Tb^{3+} , Dy^{3+} , Tm^{3+}) [9]. Owing to weak *f-f* oscillator strengths of RE ions, in order to obtain bright luminescence, a three step process is adopted in general, where in, energy absorbed by host ions is transferred to the activator ion, leading to emission of light [9].

In general, the direct excitation of Ln^{3+} ions are inefficient, owing to forbidden nature of *4f-4f* transitions. However, it is the forbidden *4f-4f* electronic transitions which offer sharp emission bands in the UV-vis range upon UV excitation [10]. Phenomenon such as energy transfer (ET) and charge transfer (CT) thus play an important role in enhancing the luminescence efficiency [11]. The sharp spectral lines owe their origin to characteristic 'shielding effect' in

TABLE 1: Basic properties of Gd based compounds

Compound		Oxide	Vanadates	Fluorides	Phosphates
Properties	Crystal structure	Cubic , Monoclinic , Hexagonal	Tetragonal	Cubic	Tetragonal, monoclinic
	Melting point °C	2420	1780	1231	...
	Thermal conductivity (W/mK)	6.2	10.1
	Phonon cut-off (cm ⁻¹)	600	805	680	...
	Band Gap (eV)	5.45	2.9	2.8	3.3
	Mol. Weight (g/mol)	362.5	272.2	214.3	252.2
	Density (g/cm ³)	~7.5	~5.3	~7.4	~5.5
	Magnetic susceptibility cm ³ /mol	53.2	...	28.6	10.3
	Bohr Magneton (Magnetic moment per formula unit), μ _B	13.997	7.000 μB	7.94	...

following selection rule, such that parity change is not involved in transitions within a configuration. Laporte's selection rules suggests that Ln³⁺ ions are primarily characterized by strong $4f^{n_i}-4f^{n_i}$ transitions in between D-F and as electron shells of $4f^{n_i}$ energy levels in RE ions have equal parity, the ED transitions (EDT) are deemed forbidden.

Meanwhile, the magnetically driven transitions (MDT) are allowed according to selection rules. Interestingly, transitions occurring in between $4f^{n_i}-4f^{n_i-15d^1}$ and charge transfer transitions ($4f^{n_i} - 4f^{n_i-15d^1L^1$, L = ligand) are partly allowed mediated by crystal field due to mixing with the odd-parity wave functions [12]. Thus, the crystal structure and local environment around a RE activator ion dictates the intensity of the EDT and MDT involved profoundly.

1.1.1 Gd based oxide and vanadate nanosystems

Investigation of ABO_3 and ABO_4 -type inorganic nanomaterials has aroused growing interest because of their peculiar crystal structure and their enriched physico-chemical properties including magnetic/ electrical driven photoluminescence performance, photocatalysis, and energy storage among others [18-21]. Gd^{3+} ($4f_7$, 8S) based host matrices are significant phosphors due to relatively high energy of the lowest excited state in connection with stability of a half-filled of the ground state [11, 22, 23]. The basic physical and chemical properties of several gadolinium based compounds are highlighted in **TABLE 1** [24-31]. Considering its high thermal stability, chemical stability and low phonon energy (phonon cut-off $\approx 600\text{ cm}^{-1}$, Gd_2O_3 acts as a promising host material for selective doping with suitable impurities including those of RE ions [32].

Various polymorphs of REOs as generated using *Vesta*[®] are illustrated in **FIGURE 1.2** viz. A-type, s. g. no. 164 ($P-3m1$), B-type, s. g. no. 12 ($C2/m$) and C-type, s. g. no. 206, ($Ia-3$) and D type structures, s. g. no. 115 ($P-4m2$) [33-35]. Of these, the C-type cubic phase is found to be stable at room temperatures, with cations positioned in six-fold coordination. Some of the reported commonly used routes for synthesis of REOs include: hydrothermal route [36, 37], sol-gel method [38], combustion synthesis [39] precipitation method [40], and chemical vapour deposition [41]. Properties such as moderate cut-off phonon energy, relatively higher- luminescence quantum efficiencies and inherent stability are common in RE orthovanadates [24, 42-46]. Among the different luminescent Gd- based compounds, gadolinium orthovanadate ($GdVO_4$) is of special interest from the optical window point of view since the excitation of the doping Ln^{3+} cation through an energy transfer from the vanadate anion is much more efficient than the direct excitation of the Ln electronic levels and is considerably effective as compared to direct excitation thereby resulting in a higher luminescence [47]. Consequently, the immensely pronounced luminescence response has relevance in fields, such as cathode ray tubes, fluorescent lamps, X-ray detectors scintillators, lasers, and amplifiers for fibre-optic communication etc. [48-51].

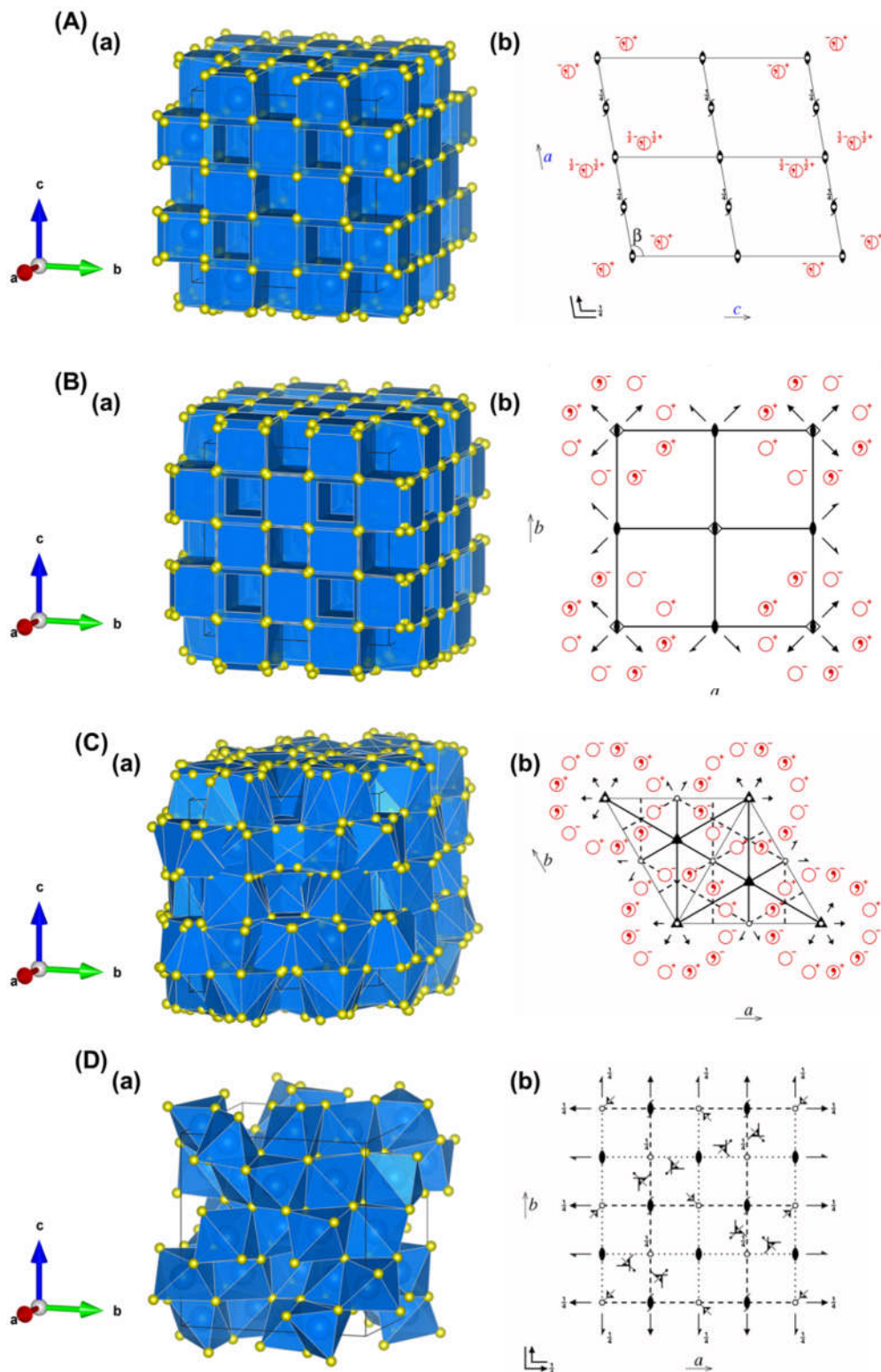


FIGURE 1.2. Unit cell structure of various polymorphs of REO with different space group no. (A) 12, (B) 115, (C) 164 and (D) 206. (b) The polyhedral unit cell structure is shown in (a) and the space group diagram. Yellow balls signify O atoms while blue balls signify RE atoms. The details of space group diagram notations can be found in Cockcroft, J., A hypertext book of crystallographic space group diagrams and tables. 1999..

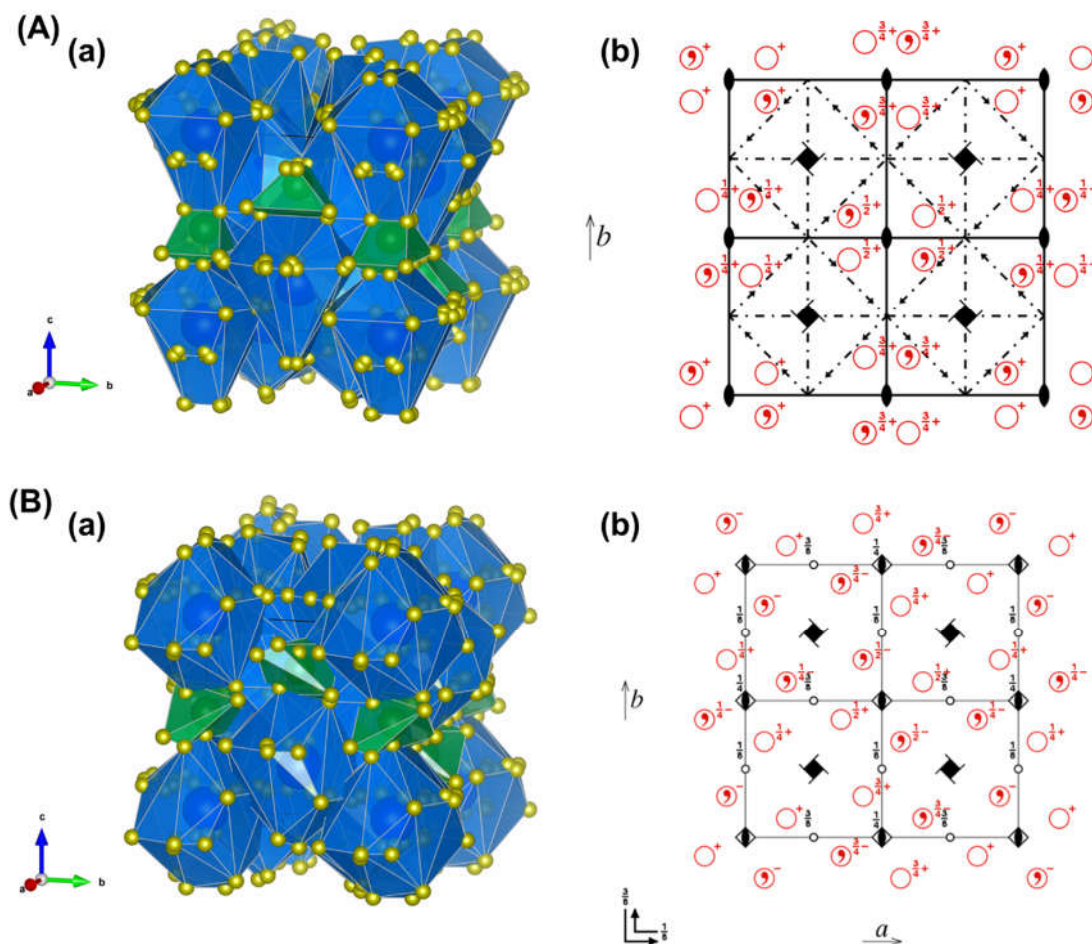


FIGURE 1.3. Unit cell structure of REV in (A) zircon and (B) scheelite type structures. The polyhedral unit cell structure is shown in (a) and the space group diagram for the respective polymorphs are displayed in (b). In the figure, yellow balls signify oxygen atoms while blue balls signify RE atoms and green balls signify V atoms. The details of space group diagram notations can be found in literature Cockcroft, J., A hypertext book of crystallographic space group diagrams and tables. 1999..

GdVO_4 represents a prototype zircon-type compound that shows a similar structure to many other zircon-type lanthanide orthovanadates (LnVO_4) belonging to the space group $I4/amd$ at ambient conditions where Gd, V and O occupy the positions $4a(0\ 0\ 0)$, $4b(0\ 0\ 0.5)$ and $16h(0\ x\ z)$, respectively [52]. Interestingly, reports suggest that zircon-type REV system displays various polymorphs under high pressure (**FIGURE 1.3**) [53]. Specifically, REV with larger ionic radii RE (Ce, Pr, and Nd) undergo a zircon-to-monazite transition, and in

the other hand, RE with smaller ionic radii (RE = Sm-Lu) transform into the scheelite-type structure [53]. In addition, Eu^{3+} doped GdVO_4 systems display scheelite-fergusonite transition as well, following minor structural changes at higher pressures [54]. The most common polymorphs for GdVO_4 are (a) zircon type (s.g. no.109), (b) scheelite type (s.g.no. 88) are demonstrated as polyhedral unit cell structures generated using *Vesta*[®] in **FIGURE 1.3**.

1.1.2. Doped RE nanostructures

In the beginning of 21st century, there has been a rapid increase in publications elaborating RE doped nanoparticles can be found [55]. The need for powerful and efficient laser source has driven researchers over the past few decades to draw their attention towards investigation of Ln^{3+} ions in various host matrices [56]. REOs and REVs are also an attractive host for incorporation of several lanthanide ions to produce efficient phosphors, emitting a variety of colours. The doped RE luminescent nanomaterials form one of the major areas of research and are regarded as promising alternative candidates to the organic fluorophores and fluorescent quantum dots [57]. The suitability and specificity of the system is determined by the choice of an appropriate matrix, usually consisting of a host oxide acting as a light absorber otherwise known as sensitizer and rare-earth light emitting ions or the activators.

Gd^{3+} emits in the UV range, restricting its usage as bioluminescent probes. Conversely, following quantum cutting or down-conversion effect, Gd^{3+} can effectively transfer UV excitation energy to Eu^{3+} species, ensuing bright red emission [58]. Meanwhile, Eu^{3+} is a technologically important dopant due to its bright red (Eu^{3+}) and bright blue (Eu^{2+}) luminescence [18, 59-62]. Europium-doped yttrium vanadate ($\text{Eu}^{3+}:\text{YVO}_4$) [63] or europium-doped gadolinium oxide ($\text{Eu}^{3+}:\text{Gd}_2\text{O}_3$) [64] are some of the reported systems which possess several distinct advantages: (i) no blinking behaviour, as large numbers of dopant ions are present in individual nanoparticles, and (ii) narrow emission bandwidths independent of particle size, which in conjunction with the use of different dopant ions and matrices, makes them suitable for multicolour labelling experiments [60]. Eu^{3+}

also exhibits well recognized pure red light-emitting centre following highly intense ${}^5D_0 \rightarrow {}^7F_2$ electronic transition [56]. The emission profile of Eu^{3+} is also important citing that it has distinct MDT (${}^5D_0 \rightarrow {}^7F_1$) and EDT (${}^5D_0 \rightarrow {}^7F_2$) transitions. MDT are allowed transitions, and are insensitive to the local environment of the activator ions. In contrary, EDT are partially allowed due to the influence of crystal field, according to Laporte's rule, and hence are highly sensitive to the local environment.

Gd^{3+} has seven unpaired electrons which makes it suitable for magnetic resonance imaging, while the $D-F$ transitions in Eu^{3+} enables it to perform extremely well as red phosphors [11, 24]. The combination of both lanthanide ions has been the basis for the development and characterization of most bi-functional contrast agents [24, 65, 66]. The cubic phase of Gd_2O_3 is rather an adequate host for suitable RE doping [32, 67]. It is the dipole interactions that lead to both electrically and magnetically driven transitions in case of RE doped RE-Oxide systems [68].

In addition, Ln^{3+} doped inorganic vanadate based phosphors, such as, YVO_4 , and GdVO_4 also have been a great deal of interest in different solid state light emitting and play an important role in development of promising laser devices [11, 69].

Furthermore, the properties of REV can be tweaked and tuned as per our requirement upon introduction of dopants into the host material, which turns them into exceptionally useful matrix materials [45]. In particular, Eu^{3+} as a dopant in GdVO_4 has proven to be a highly efficient as intense red light-emitting phosphorescent material, owing to strong absorption of UV radiation by the tetrahedral groups and effective energy transfer activator dopant Eu^{3+} ions [11, 18, 22, 45, 70, 71]. The Gd^{3+} based orthovanadate crystals display properties that allows them to be used as lasing host materials (see **TABLE 1**) [72, 73]. As a host matrix, tetragonal zircon-type gadolinium orthovanadate Gadolinium orthovanadate (GdVO_4) for RE activators was first studied by Zaguniennyi *et al.*

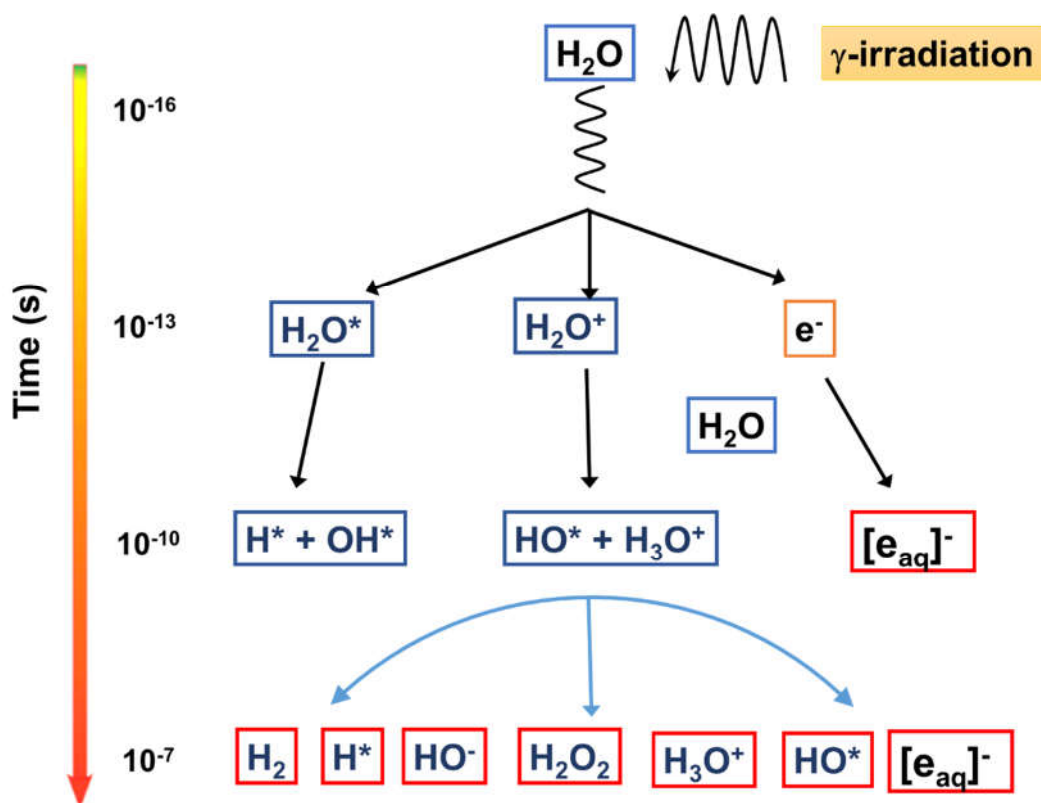


FIGURE 1.4. Radical generation in a time dependent manner upon radiolysis induced by γ -irradiation in aqueous medium.

in 1992 and shown to have superior properties compared to YVO_4 , such as higher thermal conductivity, larger emission as well as absorption cross section [74-76]. GdVO_4 doped with europium ($\text{Eu}^{3+}:\text{GdVO}_4$) has proven to be excellent red emitter, which has many applications in luminescence displays cathode ray tubes and lamps [62, 76-79]. Moreover, while most phosphors display fluorescence quenching with increasing temperature, $\text{Eu}^{3+}:\text{GdVO}_4$ have shown applications in high temperature environments for its remarkable performance [80]. Various reports could be found in literature that provide us with a detailed protocol for preparation of RE doped RE-vanadate system following solid-state cum reactions [81-83]. In addition, the long lifetimes of RE nanostructures can be exploited for easy implementation of slow detection schemes eliminating undesired signals like cell background fluorescence and direct acceptor excitation in Förster resonant energy transfer (FRET) experiments [84].

1.2 Impact of γ -radiation on RE based nanomaterials

High energy photons (γ or X-rays) have found applications in major scientific fields *viz.* nanophotonics, nuclear engineering, smart agriculture, space technology, and clinical usage [85, 86]. In general, γ -ray irradiation effects are believed to be most energetic electromagnetic radiation (energy >100 keV, frequency $>10^{19}$ Hz) and find their utility in various fields such as radiography and medical equipment's sterilization in clinical research. Also in agriculture, radiation treatment are mostly utilized for food items to extend their shelf-life by destroying harmful pathogens without affecting the nutritional values of goods [87]. Radiation treatment has a special privilege in industries producing chocolates and confectionaries. Such high radiation energy (higher than the band gap of the material) has the potential to both create as well as annihilate structural defects such as colour centres or oxygen vacancies in oxides [88]. In semiconductors, γ -rays can also ionize the electrons from their valence band maximum (highest level in the valence band) and thereby can be free resulting in generation of positive holes captured by the already present intrinsic defects [89]. Radiation exposure has a profound effect on the optical, electrical and physical properties of materials, and to the extent which primarily depends on the doses employed [90]. The degree of crystallinity and aligned orientation can be introduced at high enough doses of radiation. Reports can be found in literature which deal with the effect of radiation driven change in lattice parameters and generation/accumulation of crystal defects (point defects) on PL emission response as well as alteration of band-gap variation [91-93].

Depending on the type of interaction with matter, and photon energy, irradiation can result in either photoelectric effect, or Compton effect. Upon γ -ray irradiation of aqueous suspension, most of the energy is absorbed by water, and so water radiolysis might take place, which results in formation of reactive species such as oxidizing hydroxyl radical ($\text{OH}\cdot$) and very powerful reducing radicals [94]. The generation of radicals is time dependent as shown in **FIGURE 1.4** [94]. The interaction generates free radicals by radiolysis process which recombine or

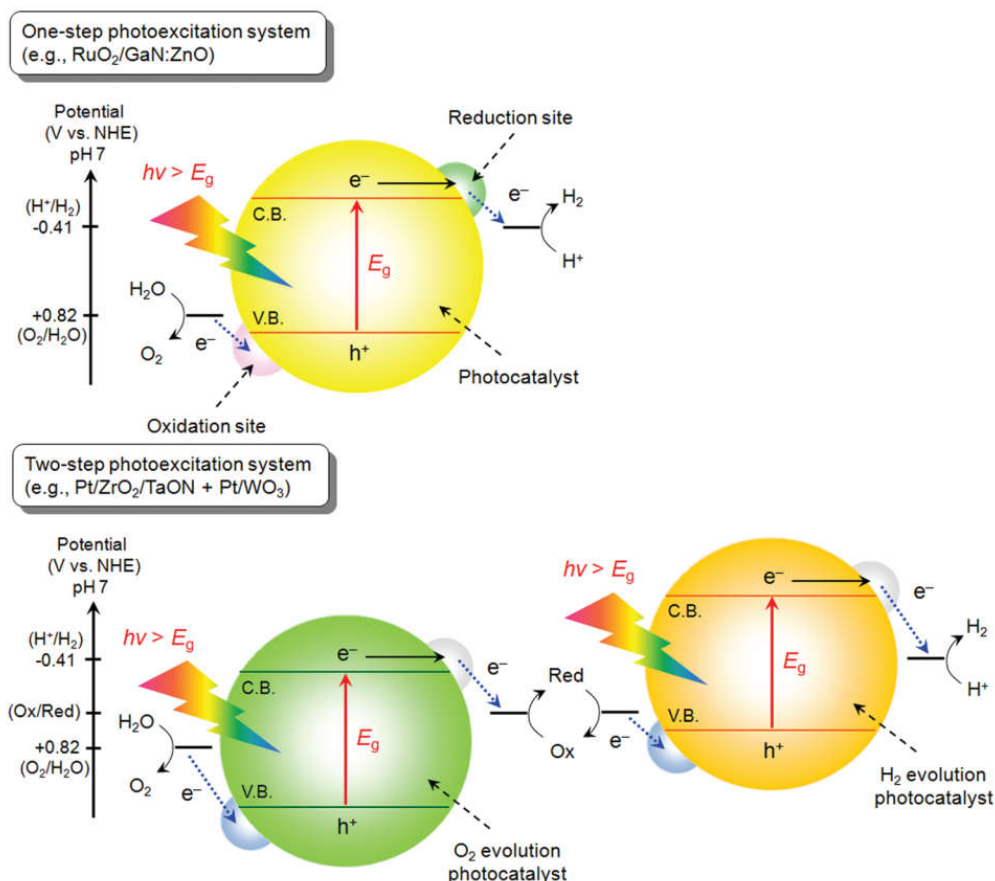


FIGURE 1.5. Illustrative description of energy schema for water splitting through photocatalytic behaviour by one-step and two-step photoexcitation systems. Here, C.B., V.B. and E_g are conduction band valence band, and band gap respectively (With permission from Maeda, K. and Domen, K., *The Journal of Physical Chemistry Letters*, 1(18)2655-2661, 2010).

interact with other species present in the solution and alter optical properties. High energetic γ - irradiation is also capable of creating and annihilating point defects in chemically stable Gd_2O_3 system as well [95, 96]. Interestingly, RE ions have displayed γ -radiation shielding properties when doped in glasses [87]. This aspect of RE ions needs to be evaluated in detail to be able to produce material that can provide safe guard towards harmful and adverse effects of γ -irradiation. Interestingly, such shielding nature can prove crucial in developing radiation resistant tools that can be advantageous in usage for space exploration and in space shuttles exposed to high amount of radiation.

1.3 RE nanosystems as photocatalytic agents

Development of novel approaches for undertaking environmental remediation of pollutants owing to unsafe and unchecked waste discharges through industrial plants and human activity needs to be encouraged [97]. Considering textile based industries and mills which are the major plants contributing to industrial wastes and pollutants in the environment, azo dyes constitute ~50-70% of all organic dyes used, which are extremely toxic as well as oncogenic [97, 98]. Conventional techniques of degradation of chromophores reportedly forms harmful by-products via processes, such as oxidation, hydrolysis, or other regular chemical reactions, leading to secondary problems [99]. *Congo red* (CR) is the first anionic synthetic azo dye, which has two azo chromophores, giving a characteristic complex aromatic structure and hence is relatively more stable than other organic dyes. Numerous reports can be found describing several techniques for degradation of azo dyes, which include- ion exchange, membrane separation or nano-filtration, usage of activated carbon, irradiation, electro-kinetic chemical coagulation/flocculation, electrochemical destruction, ozonation and photochemical degradation [100-107].

Yet most of the aforementioned general methods for photocatalysis are not economically viable as they require high-end technological interventions, and may also display disadvantages such as sludge unwanted end-products formation [102]. Incidentally, usage of nanomaterials as potential photocatalysts is worth mentioning owing to their effectual catalytic properties in water and splitting of water [108-110]. Currently, in the field of photochemistry, much efforts are being made to develop materials which could, under ambient conditions, be able to decompose water in a single step photoexcitation/recombination process under irradiation conditions [111]. The process of water splitting through photocatalytic activity following one-step and two-step photoexcitation systems can be found in **FIGURE 1.5**. [112]. In such processes the most important parameter is the gap between the conduction band, valence band or in other words, the optical band gap, E_g . In this context, the promising role of REV

nanosystem as photocatalytic agents needs special mentioning [113-116]. Theoretically, GdVO_4 exhibits the desired position of the band edges thereby promising a potential photocatalytic agent with higher ability to generate hydrogen from water or water/alcohol solutions [117, 118]. 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 [111, 118]. Reports can be found in literature that deal with possible enhancement of photocatalytic activity of a nanosystem following inclusion of metal ions as dopants [119]. RE ions as dopants have also shown to increase the activity against azo dyes under visible light illumination [120]. In particular, effects of europium doping on the photocatalytic behaviour of AVO_4 systems has been evaluated earlier and the observed augmentation in photocatalytic behaviour was ascribed due to the effective spatial separation of electron-hole following inclusion of dopants into the system [121].

1.4 Biophysical viewpoints of RE based nanosystems

NPs are sized smaller than living cells allowing interactions with internal organic structures, which can be examined *in vitro* and *in vivo*. The major applications of NPs in the biomedical research fall either in the category of imaging and/or therapeutic study. In the last few decades, abundant progress has been made in developing NP based magnetic resonance imaging (MRI) contrast agents (CA) for multimodal imaging as a diagnostic tool [23]. Gadolinium complexes/chelates are well known clinically approved imaging and therapeutic modalities, used as MRI positive CAs and anticancer chemical drugs [23]. However, such complexes have certain limitations such as shorter blood retention period and non-specific bio-distribution [23]. Nanostructured materials can be employed to overcome these limitations. In the past few decades we have witnessed, great potential of lanthanide (Ln^{3+})-doped nanostructures in the biomedicine field owing to their unique optical and magnetic characteristics [18, 122]. Furthermore, in the line of the studies devoted to the development of nanoparticles for diagnostic

applications, cancer therapy based on nanostructures has recently received much attention, since their small size facilitates their accumulation in tumours [123, 124].

In terms of their usage in biological field, nanoparticles are attractive not only for their small dimensions but also for their greater diversity as regards shape composition, which allows one to envisage many complementary strategies for tumour destruction [125]. Two main classes of particles can be distinguished according to their mode of operation: particles can be used (a) to deliver drugs as drug delivery systems (DDSs) to the cancerous cells [61, 126] and (b) to induce the tumour annihilation after adequate interaction with an external physical stimulus [127]. Many routes are currently being explored in order to incorporate a large number of drugs inside or onto the nanoparticles as a means of oral and intravenous administration [126]. RE doped Gd_2O_3 nanostructures also have vast implications with regard to drug delivery [61]. Gadolinium-based nanomaterials have moved into the spotlight as efficient magneto resonance imaging (MRI) contrast agents for bio-imaging and effective nano-vehicles for chemotherapy [128, 129]. Reports can be found with Gd based nanoparticles treated as potential cancerous cell labelling agents, thereby proving its role in diagnosis further than MRI CAs [130]. Bridot *et al.* proposed usage of Gd_2O_3 NPs as T_1 contrast agent and showed that presence of Gd^{3+} ions could enhance relaxation time [131]. Fluorescence imaging is an appropriate tool with respect to MRI in areas of higher sensitivity, quicker acquisition and easier handling for monitoring the uptake by cells.

Moreover, owing to the crystalline nature of cubic Gd_2O_3 NPs, the number of Gd^{3+} ions per particle is relatively high (about ~ 200). As a result, the accumulation of these particles in cancerous cells is expected to have immense potential for Gd based anti-cancer therapeutic use [131]. Such particles appear therefore, very attractive, because they could combine dual modality, namely, imaging and therapy [132]. The NP DDS have the prospective to improve current therapies as for their ability to overcome multiple biological barriers and

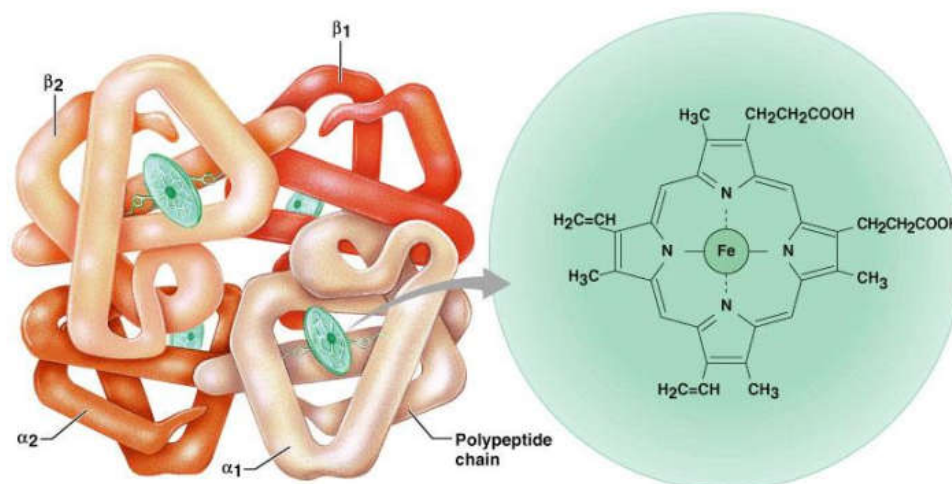


FIGURE 1.6. Illustrative diagram displaying the four polypeptide chains attached to heme group in a haemoglobin (With permission from RBC Marieb, E.N. and Hoehn, K. Human anatomy & physiology. Pearson education, 2007).

thereby releasing a therapeutic load in the optimal dosage range to a requisite site [133].

It is worth mentioning that in order to develop biocompatible NPs, it is essential to systematically evaluate and understand the nano-bio interface, more relevant to the cellular uptake mechanisms. One of the major concerns in chemotherapy is the toxicity of the drug to be administered [134]. Targeting allows prohibition of unwanted side effects on healthy parts of the organism, so that the active principle can be delivered at higher concentrations to selective region for treatment. For a target-oriented delivery of the active compound, the latter has to be conjugated with an addressing moiety [135]. Investigation of the interactions of NPs and cells *in vitro* offers a quick and convenient approach to explore the cellular responses to specific NP dose, exposure time, and intracellular NP fates with specific cell types. Beneficial usage of nanoparticles (NPs) can be realized only if their potentially harmful and adverse effects are studied in great detail with due emphasis on their interaction at the nano-bio interface. Important biochemical as well as biophysical mechanisms occurring at the nanoscale hence requires our careful attention [136, 137]. Reports describe that nanoparticles can

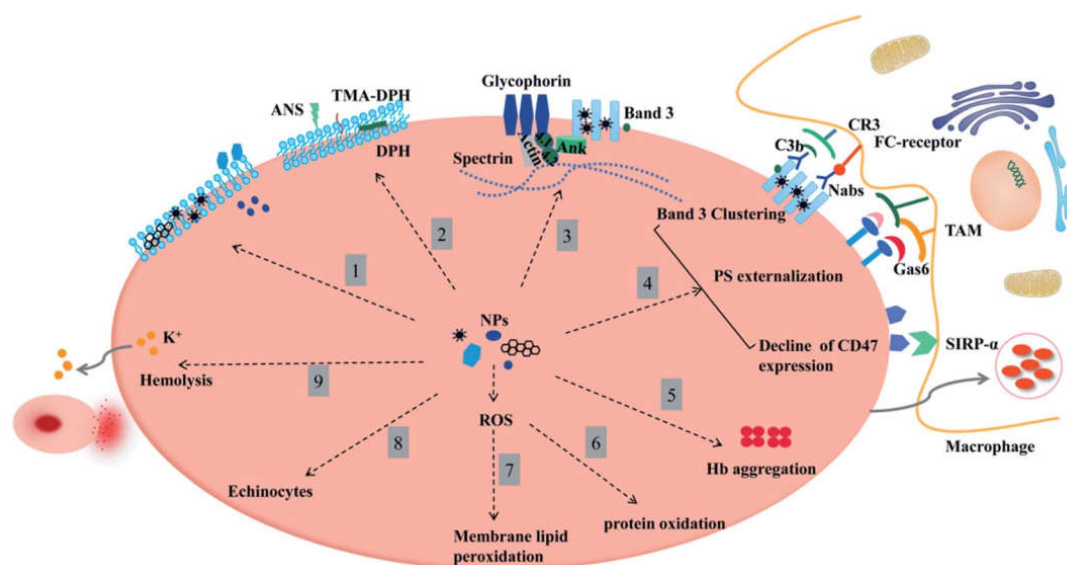


FIGURE 1.7. A graphical representation summarizing consequences of NP-erythrocyte interaction. (1) NPs penetrate the cell membrane bilayer to enter the cell. (2) NPs disturb the cell mobility (3) NPs can cause functional damage to band 3 membrane structural proteins and spectrin, band 4.1, and 4.2 proteins or actin. (4) Band 3 protein clusters can be formed, and decrement of CD47 expression can trigger activation of macrophage phagocytosis. (5) Aggregation of hemoglobin (Hb) can take place. (6 and 7) Membrane lipid/protein peroxidation can occur. (8 and 9) Erythrocytes can transform into echinocytes, and as a final point turn up to be hemolyzed (either partially or fully). (With permission from Tian, Y., *et.al.* RSC advances, 11(12)6958-6971, 2021.)

be translocated from the lungs into the blood hence can be responsible to cause oxidative stress-mediated toxicity [137, 138].

Strikingly, NPs can pose various hemotoxic threats *via*. processes such as hemolysis and/or blood coagulation [139]. This feature cannot be overlooked as in case of intravenous administration, Gd based NPs would initially be exposed to blood and hence requires special care and handling. The NP-erythrocyte interaction involves factors such as activation, aggregation and adhesion of platelets, ultimately lead to membrane rupture and are complemented by shape transformation of red blood cells (RBCs) in addition to reactive oxygen species (ROS) generation [140, 141]. Such loss of erythrocyte membrane integrity or hemolysis envisages hemoglobin release through ruptured cells [139]. A normal

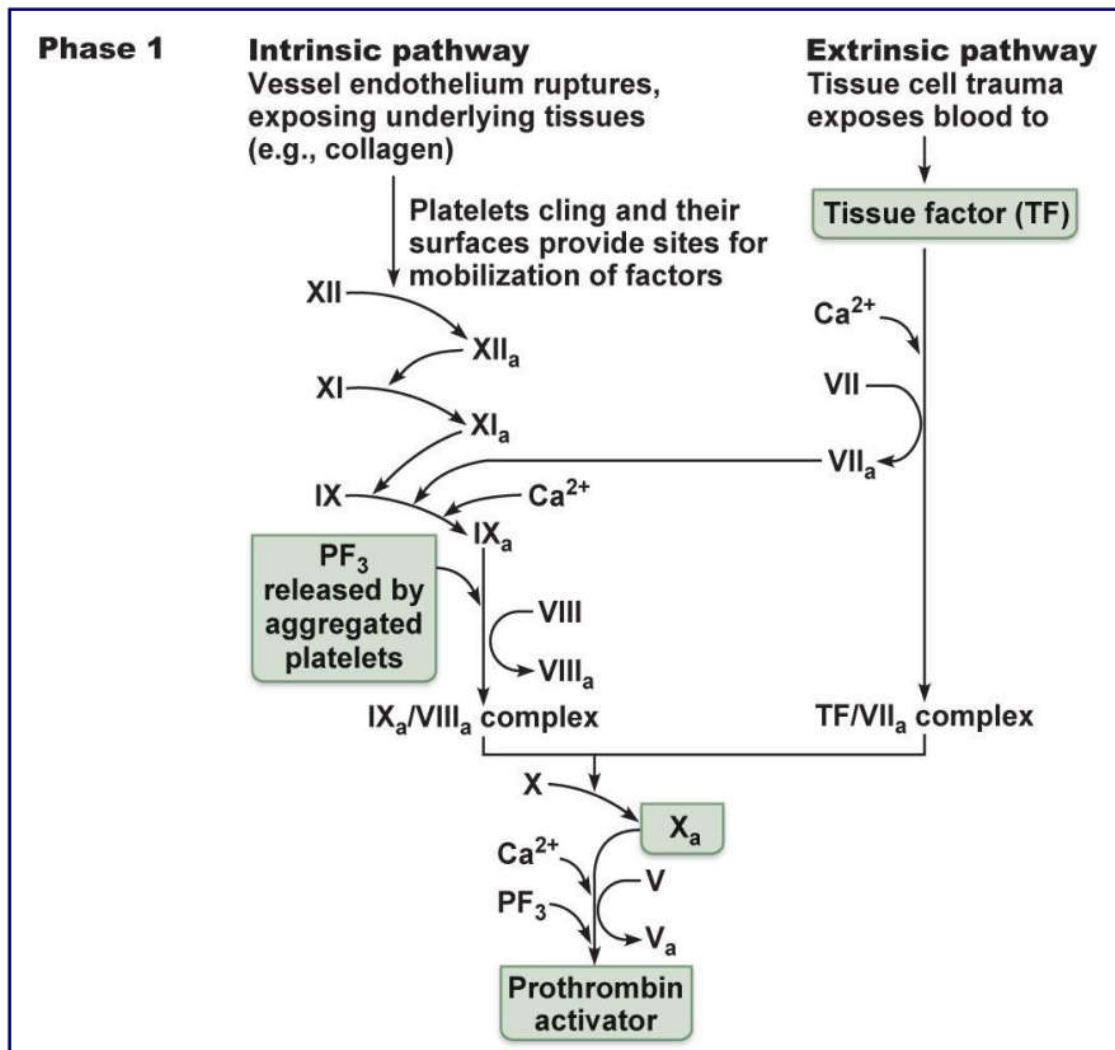


FIGURE 1.8. Coagulation cascade following the extrinsic and intrinsic pathway. involving various coagulation factors as described in Marieb E.N. and Hoehn K. Human Anatomy and Physiology. San Francisco, Pearson Education Inc., 2010. (With permission from Alkinany, A.S., Introduction to Human Physiology.

healthy erythrocyte is crucial for achieving deformability necessary for cell survival [142]. The inner leaflet is negatively charged which generates a substantial charge difference between the two leaflets [143]. The overall contents of the RBCs lie enclosed within these leaflets by means of a network of cytoskeletal and membrane proteins while other cytoplasmic structures & membrane skeleton (MS), is a 2D cross-linked protein cytoskeleton lies inside the plasma membrane [142, 144, 145]. Hemoglobin (Hb), contains four polypeptides chains (2 α & 2 β globin chains) with a heme attached to each chain as shown in the **FIGURE 1.6**

[146]. The heme carries oxygen transporting iron atom pigment [147]. NPs led damage to RBCs leading to hemolytic effects can also be mediated through alterations in rheological properties, oxidative damage of cell membranes, imbalance of osmotic stability etc. [148].

In general, RBCs are treated as a model of non-phagocytic cell which have the ability to undergo shape transformation and hemolysis and hence is extensively used to approximate the cytotoxicity of both natural and synthetic compounds [149-151]. Thorough investigation of change of erythrocytic shapes is a classic problem in the domain of cell biology and over the past three decades, the domain has also fascinated the physicists working for explaining biophysical processes [145]. Human RBCs are treated as prototypical cells in order to have an in-depth investigation of effects such as shape transformations and nanoparticles-cell membrane interaction using Scanning Electron Microscope (SEM) [141, 152]. Morphological transformations of erythrocytes can also be used for evaluating the hemocompatibility of nanomaterials [139]. **FIGURE 1.7** summarizes effect of NP interaction with erythrocyte effecting its morphology, and function [153]. Such irreversible alterations affect membrane morphology [153].

NPs have also displayed adverse physiological changes and biological functions [154]. Coagulation can be stimulated through extrinsic or intrinsic pathway (**FIGURE 1.8**). These coagulation factors usually remain in their inactive states and are triggered by complex chemical reactions influenced by Ca^{2+} ions, several phospholipids and also factor V. In this regard, application of Gd based NPs as a nanomedicinal agent has to be administrated carefully because Gd^{3+} ions reportedly have the potential to replace of Ca^{2+} in some calcium (II) binding sites [155]. Furthermore, adsorption of phospholipids on the MRI contrast agent surface can also take place forming protein corona over the nanoparticles [156]. Hence, evaluation of plasma-NP interaction, in addition to hemocompatibility, needs attention for effective design of a theranostic agent.

1.5 Thesis objective and structure

This thesis provides a detailed account directed towards development of a multimodal luminescent material capable of displaying stronger emission profile, longer decay lifetimes as well as presents biocompatible features. Gd based oxide and vanadate nanostructures incorporated with Eu^{3+} activator ions have been evaluated for optimal luminescence with high emission intensity profile for moderate doping and below quenching concentrations. In order to achieve asymmetry around activator ions, effect of defect creation due to 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. This thesis is segregated into eight chapters with the necessary relevant references listed at the end of each chapter in a separate chapter.

The principal features of Gd_2O_3 and vanadate GdVO_4 systems are discussed in '*Chapter I: Introduction*' of the thesis. The energy level diagram and characteristic processes involved in RE based nanosystems, such as 'Shielding effect' are demonstrated. An extensive literature survey regarding their PL properties and applicability as nanophosphors has been elucidated. Moreover, the nanotoxic nature of the systems focusing their potential usage in biological applications as a theranostic agent has been reviewed with relevant citations.

The synthesis protocol implemented for preparation of nanosystems are highlighted in '*Chapter II: Synthesis and basic characterization of Gd_2O_3 and GdVO_4 nanosystems*'. Crystal phases are confirmed following the X-Ray diffraction (XRD) analysis. Transmission electron microscopy (TEM) imaging based visualization of the nano-crystalline features are also made along with the determination of optical band gap using UV-Vis spectroscopy. X-ray Photoelectron Spectroscopy (XPS) based surface revelations are also included in the chapter.

The '*Chapter III: Influence of dopants and γ -irradiation on radiative events of $\text{Eu}^{3+}:\text{Gd}_2\text{O}_3$ nanosystems*' highlights identification and probing of relevant

transitions observed in the PL profile of Eu^{3+} , in order to associate the electrically driven (ED) and magnetically driven (MD) transitions involved. The effect of γ -irradiation on the emission profiles are studied in detail and are described accordingly. Moreover, manifested luminescence features upon introduction of co-dopants in the nanosystem of varied morphology is also designated. A thorough analysis of time resolved photoluminescence aspects was made employing time correlated single photon counting (TCSPC) capability (Horiba, USA). Phosphorescence decay parameters were also evaluated following radiation exposures at varying doses as well as dopant concentration.

'Chapter IV: γ -irradiation induced PL quenching in $\text{Eu}^{3+}:\text{GdVO}_4$ nanosystems and related phosphorescence decay dynamics' describes the effect of dopant concentration and γ -irradiation on tetragonal $\text{Eu}^{3+}:\text{GdVO}_4$ with special attention relevant to impact on lifetime features.

In *'Chapter V: Raman characteristics of $\text{Eu}^{3+}:\text{GdVO}_4$ nanosystems'*, manifestation of Raman active modes and effect of dopant concentration on Raman spectra of $\text{Eu}^{3+}:\text{GdVO}_4$ is presented. Observation of partial phase transition from *Zircon* to *Scheelite* type crystal structure upon inclusion of dopants in the nanosystem is discussed in detail.

In *'Chapter VI: Effective photocatalytic activity of nanoscale $\text{Eu}^{3+}:\text{GdVO}_4$ on Congo Red (CR) dye'* the photocatalytic performance of the as-derived nanocatalysts against azo dye-CR has been highlighted considering daylight and UV illumination. The characteristic absorption spectra of CR dye are analysed carefully and the excellent dye removal efficiency of $\text{Eu}^{3+}:\text{GdVO}_4$ under white light and UV light illumination is demonstrated adequately.

'Chapter VII: Bio-relevance and hemocompatibility of $\text{Eu}^{3+}:\text{Gd}_2\text{O}_3$ and $\text{Eu}^{3+}:\text{GdVO}_4$ nanosystems' highlights biocompatible features of the nanosystems with special reference to hemocompatibility. The chapter includes determination of hemolytic activity and analysis of effect of plasma-NP interaction on plasma recalcification time (PRT) in human blood. Moreover, a description of

morphological transformations leading to hemolysed RBCs is presented with the help of high resolution SEM imaging.

Finally, 'Chapter VIII: Conclusions and future aspects' of the thesis summarizes the observations made following the investigations performed using different tools and techniques. The important findings are highlighted along with their scope relevance in future studies.

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