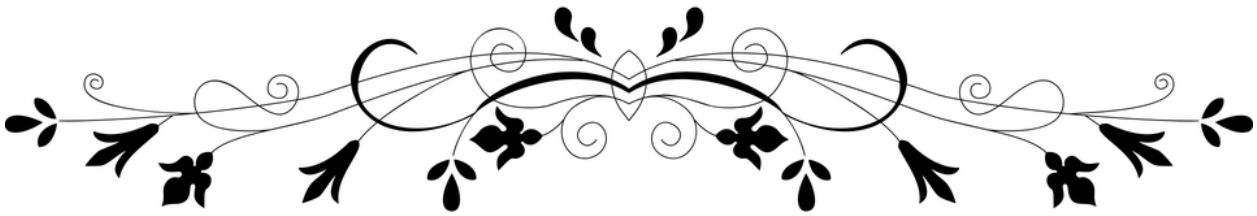

CHAPTER 7

Summary of research & scope of future work

CHAPTER 7

7.1 Summary of the Work

In summary, it is concluded that for multifunctional applications in the field of cancer theranostics and other diverse physicochemical sectors like electrochemistry and magnetism, nanomaterial synthesized using the green route would be a viable alternative. Medicinally acclaimed and common food supplement entity like *M.oleifera* plant holds strong potential to expedite the process synthesis of photo-physically active nanomaterials based on copper based biominerals and rare- earth-doped UCPs. Copper biominerals such as Atacamite and Copper oxide chosen in this research are suitable enough for possible cancer theranostics application by virtue of their modulated thermal energy generation and optical activity. Additionally upon nanoscale size reduction they projected to have astounding luminescence property, electrochemical and magnetic activity for simultaneous usability in other physicochemical areas. These type of biominerals having biological origin, successfully testified to have antifungal and bactericidal applications, but never been explored in advance cancer theranostics field. Though they are reported to be cytotoxic towards cancerous cells when used as chemotherapeutic drug. However, in order to alleviate the limitations associated with chemotherapeutic treatment such as in-effective bio-distribution of drug molecule and cytotoxicity to healthy tissues, there is growing demand for advance treatment therapy and imaging modalities. State of the art nanomaterials, endowed with both multimodal imaging and advanced therapeutic facility not only effective in ascertaining the exact physiology of tumor tissues but also assist in subsequent image-guided therapy. From the imaging prospect fluorescent and MRI based diagnostic systems have superioty over conventional ionizing radiation in terms of resolution, practical achievability, safety etc.

Furthermore photothermal therapy is an important cancer treatment technique effective in the hypoxic and necrotic region of tumor tissue unlike limitations imposed by several advanced cancer treatment modalities. Based on the interesting photo-physical attributes of both Atacamite and Copper oxide nanomaterials, they are suitable enough for development of above discussed multifunctional cancer theranostics agent. Besides Copper-based biominerals, luminescent thulium-doped UCPs also have superiority in terms of optical property and thermal energy generation ability. Hence appropriate enough for advance cancer theranostics application, mitigating the limitations aroused from conventional chemotherapeutic drug and radiation based imaging systems. Additionally, a high signal-to-noise ratio, no unprecedented external interference, unpaired electrons further enable trivalent thulium-doped UCPs for concurrent applicability in various analytical and magnetism-related applications as like copper biominerals. *M.oleifera* leaf extract in combination with hydrothermal reaction condition mimics the natural mineralization process that ultimately produced the above-discussed copper biominerals and thulium-doped UCPs with tunable morphology & crystallinity in a facile manner. Further, this technique also facilitates a single-step mechanism under which developed nanomaterials are simultaneously endowed with both surface functionalities, as well as biocompatibility for performing above discussed theranostics and physicochemical functions. In continuation with above discussed feasibility of hydrothermal reaction in combination with plant extract, nanoclusters of Atacamite have been successfully synthesized. This is first of kind research of its type where ultra-small sized (~2 nm) nanoclusters of Atacamite synthesized in lab scale using green route. Moreover these small sized structure with plasmonic band transition successful enough for *in Vitro* killing of MG-63 osteosarcoma cell lines upon 975 nm laser exposure (η= 20.7%). Use of *M.oleifera* leaf extract also assist in modulating the optical property of

developed semiconducting nanostructures and imparting them fluorescence character for successful end use in *Drosophila* salivary gland tissue imaging. Further, this green synthesis method has imparted multi functionalities to these developed nanoclusters via the development of superparamagnetic characteristics. The effectiveness of above hydrothermal synthesis further extended towards development of very small sized spherical Copper oxide nanoparticles (< 13 nm). The diverse functional features of developed nanoparticles have been successfully used for the photothermal killing of B16F10 melanoma cell lines grown in Vitro. Additionally, investigation regarding electrochemical properties of developed Copper oxide nanoparticles resulted in interesting results in terms of electrochemical active surface area, specific capacity, and charge storing delivering ability. Specifically, the improved electrochemical active surface area (~0.13 cm2), high specific capacity (~247.25 F/g), and striking balance between high energy (~21.11Wh/Kg) and power density (~14000 W/Kg) value have made Copper oxide nanoparticles suitable candidates for charge storage and bio-analytic device fabrication. Interestingly successful usability of these green synthesized plasmonic Copper oxide nanoparticles in photothermal destruction of cancer cell lines is the first time being reported.

On contrary to above discussed biominerals the sharp luminescence intensity and NIR to heat conversion capacity are the reasons for thulium-doped NaYF4 UCPs reasonable preeminence in multifunctional cancer theranostics field. In view of possible biological usage facile hydrothermal technique involving *M.oleifera* leaf extract also adopted for synthesis of UCPs excluding toxic high boiling chemical reagents. The conventional solvo-thermal and high-temperature thermal decomposition methods are not only expensive but require additional ligand exchange mechanism for imparting surface functionality. The synergistic combination of *M.oleifera* leaf extract and hydrothermal

reaction adopted in this research mediate the nucleation and stabilization process of developed Upconverting phosphors due to abundance of long-chain fatty acid ester and phenolic compounds. As a result morphology and crystallinity tunable nanophosphors are generated. Rapid phase transformation from less efficient cubic to desirable hexagonal phase at a temperature ~170 ^{o}C is the biggest achievement of this green synthesis process. Generally growth of Upconverting crystals are based on dissolution recrystallization mechanism and efficient hexagonal phase generated at a temperature above 600 ^{o}C carried over long reaction duration. But by adopting this green synthesis method unusual results are obtained and most efficient pure phase hexagonal nanocrystals are obtained within two hour of synthesis. Though photothermal conversion efficiency (~3%) in the synthesized nanophosphors is low but the heat generation capability of 1.15 ^{o}C/min upon NIR absorption is sufficient enough for photothermal treatment application. Infact it is better than other reported UCPs in which polydopamine (PDA) was used for infrared radiation absorption. Further the synthesized Tm^{3+} doped nanophosphors are observed to be superparamagnetic in nature which is very much surprising from the Upconversion point of view. Nevertheless the green synthesis of UCPs is a preliminary study that requires rigorous modifications in terms of morphology, physical properties for successful biomedical applications.

Keeping in view above cited demands during synthesis of UCPs, hydrothermal technique adopted in this research mandates some modification in the reaction process. By following this practice we varied the nature of chelating ligands and substrate to assist the hydrothermal reaction during synthesis of thulium-doped UCPs. Chelating agents mainly used DTPA, EDTA and EGTA those have different extent of coordinating capability towards rare earth ion. Similarly, substrates used namely PG, FTO and ITO have differences in terms of their surface charge, and previously reported to play pivotal

role in altering morphology and crystallinity of developing UCPs. The synergistic combination of both chelating agent and substrate has produced UCPs with diverse morphology, size and crystallinity. Further the magnitude of luminescence intensity also varied depending upon precursor combination used. To gain an insight into the underneath mechanism modulating optical property, size and morphology, investigation has carried out to evaluate the lattice strain within developing crystal. The correlation between reaction conditions and overall property modulation systematically investigated via quantification of both macro and micro strain. This study is unique in terms of its synthesis mechanism, capable of generating both UCPs and analytic platforms with desired morphology and luminescence character. As a whole the mechanistic method to quantify the lattice strain associated with the developed crystal structure and tuning of the photo-physical properties indeed a newer approach for possible biological and bio-analytical applications.

Overall we can state that the entire research has revealed the magnificent role of *M.oleifera* leaf extract in lab scale mineralization process for production of very small sized and morphology tunable copper biomineral and rare earth doped $NaYF_4$ nanomaterials. The leaf extract not only act as stabilizing or nucleating agent in order to control morphology, size and crystallinity of developed nanomaterials but also has imparted them advance photo-physical and magnetic characteristics. These attributes successfully examined in cancer theranostics and other applications such as electrochemical energy storage and MRI contrasting agent. Moreover for prioritizing the astounding photo-physical functions of the developed nanomaterials and their practical applications in other diverse sectors, some key points have been highlighted. These points should be considered as future prospect of the developed multifunctional copper biomineral based and thulium-doped Upconverting phosphors.

7.2 Future Scope

- The antimicrobial potency of copper biomineral based nanostructures and Tm^{3+} doped $NaYF_4$ Upconverting phosphors should be examined analogous to their other polymorphs.
- The nano-enzymatic activity of Atacamite and Copper oxide nanostructures should be investigated in full potential in the budding field of electrochemical biosensor.
- The theranostic efficacy of above discussed Upconverting and semiconducting biominerals, should be studied extensively *in Vivo* manner by using mouse model.
- Both copper biomineral based nanostructures and thulium-doped Upconverting phosphors should be employed in energy harvesting applications like fabrication of dye sensitized solar cell (DSSC).
- A noble lab-on–chip sensing platform should be developed for detection of biomolecules and organic pollutants using luminescence resonance energy transfer (LRET) mechanism involving Upconverting phosphors due to their stable emission characteristics.