Dedication

I greatly indebted towards the people of my country India, those paid the cost of this study and am dedicating this Ph.D. thesis to them.

CERTIFICATE

It is certified that the work contained in the thesis titled "**Green Synthesis of Copper-Based Biominerals and Rare-Earth Doped Luminescent Nanomaterial for Multifunctional Applications**" by **Kedar Sahoo** has been carried out under my supervision and that this work has not been submitted elsewhere for a degree.

It is further certified that the student has fulfilled all the requirements of Comprehensive Examination, Candidacy, and SOTA for the award of Ph.D. Degree.

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DECLARATION BY THE CANDIDATE

I Kedar Sahoo, certify that the work embodied in this Ph.D. thesis is my own bonafide work and carried out by me under the supervision of **Dr. Manoj Kumar** for a period from **July 2016 to December 2021** at the Department of Chemical Engineering & Technology, Indian Institute of Technology (Banaras Hindu University), Varanasi. The matter embodied in this thesis has not been submitted for the award of any other degree/diploma. I declare that I have faithfully acknowledged, given credit to the research workers wherever their works have been cited in my work in this thesis. I further declare that I have not wilfully copied any other's work, paragraph, text, data, results, etc. reported in the journals, books, magazines, reports, dissertations, thesis, etc., or available at websites and have not included in this thesis and have not cited as my own work.

Date:

Place: IIT (BHU), Varanasi **Kedar Sahoo**

CERTIFICATE FROM THE SUPERVISOR

It is certified that the above statement made by the student is correct to the best of my knowledge.

Dr. Manoj Kumar
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Head of the Department

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Place: IT (BHU), Varanasi (Kedar Sahoo)

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List of Abbreviations and Symbols

Abbreviation	Nomenclature
MFN	Multifunctional nanomaterial
GSA	Ground state absorption
ETU	Energy transfer Upconversion
UCP	Upconverting phosphors
UPCN	Upconverting nanophosphors
FANC	Fluoroscence Atacamite Nanoclusters
SEFANC	Silica-encapsulated fluorescence Atacamite nanoclusters
B.F.	Bright Field
V.B.	Valence band
C.B.	Conduction band
SPR	Surface plasmon resonance
ESI-MS	Electrospray Ionization Mass Spectrometry
CONP	Copper oxide nanoparticle
W.H.	Williamson-Hall
CIE	International commission on Illumination
MTT	(3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide)
MPMS	Magnetic Properties Measurement System
MRI	Magnetic Resonance Imaging
GC-MS	Gas Chromatography Mass Spectrometry
EDLC	Electrostatic double layer Capacitance
CV	Cyclic Voltammetry
EIS	Electrochemical Impedance Spectroscopy
ECSA	Electrochemical Active Surface Area
GCD	Galvanic Charge-Discharge

Symbols	Nomenclature
cps	Counts per second
a.u.	Arbitary Unit
ns	Nano seconds
^{o}C	Degree centigrade
IC_{50}	Half Maximum Inhibition Concentration
η	Photothermal conversion efficiency
I_{CP}	Cathodic peak current density
W/cm^2	Watt per centimetre square
C_S	Specific capacitance

Preface & Thesis Organization

Multifunctional nanomaterials are widely acclaimed in biomedicine, especially in cancer-related diseases, for effective diagnosis and treatment therapy. Further, by virtue of improved physicochemical characteristics via crystallinity & morphology tuning and quantum confinement effect, there are likelihoods of broad application prospects in other vital fields of electrochemistry, magnetism, photo-reduction of pollutants, and optoelectronics.

The optimized interplay between nanostructure, surface-functionalized ligands, diagnostic realm, and therapeutic agent in a multifunctional nanostructure resulted in advanced theranostic modalities for cancer disease. In order to mitigate the disadvantages and complexity associated with conventional tumors diagnosis techniques such as PET, SPET, and CT, multifunctional nanomaterials are endowed with advanced diagnostic functions such as optical imaging and MRI. Optical imaging in synergism with MRI resulted in highly resolute, multicolor anatomical images of tumor tissue, excluding the use of hazardous radio-isotopes. Further toxic effects of chemotherapeutic drugs as well as ionizing radiations to surrounding healthy tissues and the inability of photodynamic therapy to effectively act in the hypoxic/necrotic regions during tumor treatment led to an advanced therapeutic practice called photothermal therapy (PTT). Multifunctional nanomaterials with modified physicochemical and plasmonic characters act as efficient NIR to heat conversion agents, causing localized destruction of tumor tissues without hampering the physiology of healthy cells. Moreover, altered physicochemical attributes via crystallinity, size, and morphology control expedite broad applicability in other diverse sectors of luminescence, electrochemical energy storage, and magnetism. Generally, multifunctional nanomaterials synthesized from noble metal-based semiconductors are suitable enough for demonstrating above discussed qualities. In this context, copper metal, due to abundant availability and facilitation of functions like smooth transport of conduction electrons, minimum joule heating, surface plasmon polariton (SPP) wave propagation, is an appropriate material of choice for the synthesis of semiconducting multifunctional nanomaterial. Especially nanostructures of copper oxide or hydroxide-based biominerals exhibit fluorescence via quantum confinement, modulate generation of thermal energy by controlled release of covalently bound valence electrons, and paramagnetic in nature. Hence gained enhanced interest in the field of the multifunctional theranostic nanostructure. However, a limited amount of research on copper biominerals reported until now, those focused on harnessing various functional features from a single unified nanostructure. Specifically, concurrent fluorescent imaging and photothermal ability directed towards cancer theranostics along with additional electrochemical or magnetic activity are scarcely reported.

Furthermore, for the multitude of applications like cancer theranostics and probable bio-assay of cancer biomarkers, deep tissue penetrability, luminescence stability, and improved signal-to-noise ratio are some issues that need to be taken care of. Rare earth-doped multifunctional UCPs can successfully address all such issues. Owning to NIR excitation capability, high contrast optical signal, and greater amount of heat generation via non-radiative relaxation Upconverting phosphors have great prosperity in the successful theranostic aspect of deep-lying tumor tissues as compared to semiconducting biominerals. Besides unpaired electrons of doped rare-earth ions, longer luminescent lifetime, uninterrupted optical intensity, and unique signaling mechanism are major features of Upconverting crystals suitable for innovative analyte sensing mechanisms, magnetism, and optoelectronics.

Nonetheless, both morphology and size govern the fundamental dynamics of the distribution of the above discussed inorganic multifunctional nanomaterials, their effective delivery at the diseased site, and facilitating their smooth renal clearance too. However, improved theranostic functions of inorganic multifunctional nanomaterials can be interlinked with surface functionalized ligands or biomolecules that hold a solid capability to bind with overexpressed receptor moieties on the tumor surface. Surface modification with ligands is also responsible for the stability and solubility of the nanomaterial besides diverse functionalities in physicochemical, spectroscopic, and magnetism-related fields. But inorganic nanomaterials reported till now, are synthesized on a lab-scale by using toxic and expensive templates and nucleating agents followed by complex surface engineering mechanisms. Hence, an environmentally benign and facile synthesis approach is inevitable for successful use in cancer theranostics and other widespread applications.

The current thesis work has been conceptualized keeping in view the above-discussed aspects of multifunctional nanomaterial research for efficacious theranostics and physicochemical usage. This thesis is designed according to the article style format laid down by the chemical engineering department of IIT (BHU) Varanasi. The thesis consists of seven chapters, with the first two chapters devoted to the introduction and literature review & objective section. Four out of the remaining five chapters extensively discussed different aspects of multifunctional nanomaterials synthesized via environmentally benign green route and end applications in theranostics and other physicochemical sectors. The last chapter belongs to the summary of the overall research.

Moreover, the entire thesis organization is briefly discussed below:

Chapter 1: This chapter deals with the wide prospects of multifunctional nanomaterials in the diverse field of cancer theranostics, electrochemistry, and magnetism related applications. Further aptness in material selection, adopted techniques during synthesis of the multifunctional nanosmaterials, their requisite morphological & physicochemical characteristic and surface functionality aspect also highlighted. Special emphasized given to the superiority of inorganic nanomaterials based on copper biomineral and rare earth doped Upconverting phosphors.

Chapter 2: This chapter consists of an extensive literature survey related to multifunctional aspects of two copper-based biominerals, namely atacamite and copper oxide. The investigation has also been carried out to extract the reports regarding possible multifunctional attributes of trivalent thulium-doped Upconverting phosphors. Unfortunately, most reported articles are not concerned about the cost-effective and biocompatibility aspect of synthesized nanomaterials for possible biological use. Moreover, researches are centered on the mono-functional traits of these excellent nanostructures. Thus, specific objectives have been framed out to mitigate the unwanted drawbacks and for successful theranostic and physicochemical applications.

Chapter 3: This chapter reported the successful green synthesis of atacamite nanoclusters using leaf extract of *M.oleifera* plant. This is the first of kind report for this important biomineral where generation of such ultra-small dimension led to modulation in the photo-physical and magnetic characteristics. These synthesized nanoclusters are successful enough for imaging *Drosophila* salivary gland tissues and photothermal destruction of MG-63 bone cancer cells.

Chapter 4: Extending the lab-scale biomineralization process further, this chapter describes the successful synthesis of spherical shaped (< 14 nm) copper oxide biomineral.

Synthesized nanoparticles are successfully applied for the photothermal destruction of B16F10 melanoma cell lines due to their inorganic band structure and plasmonic character. Further, these nanoparticles are investigated for their potential applicability in the field of the electrochemical energy storage process.

Chapter 5: Unlike chapters 3 and 4, chapter 5 is wholly devoted to the synthesis of trivalent thulium-doped $NaYF_4$ Upconverting phosphors by employing *M.oleifera* leaf extract as a probable nucleating agent. This work is the first of its kind where plant extract produced phase pure hexagonal phase merely at 2h of time duration under a low reaction temperature, unlike lengthier process involving high boiling corrosive solvent. Synthesized nanophosphors are investigated for their photothermal heat generation capability and super-paramagnetic characterstics.

Chapter 6: Trivalent thulium-doped Upconverting phosphors, with tunable morphology, crystallinity, and luminescence ability successfully synthesized by the variation of the essential reaction elements such as chelating ligands and substrates. This chapter is designed in the prospect of understanding the fundamental dynamics nanophosphors synthesis from a mechanistic point of view. Further, this process enables production of Upconverting phosphors as per requirement (morphology and luminescence), which is crucial in the applications like cancer biology and bio-analytics.

Chapter 7: This last chapter summarizes the entire research work in a nutshell and highlights the major upshot of every chapter for achieving the objective of the whole research in a collective manner. Also, future recommendations have been made to carry forward the multifunctional research in other advanced fields like optoelectronics, analyte sensing, photocatalysis, etc.