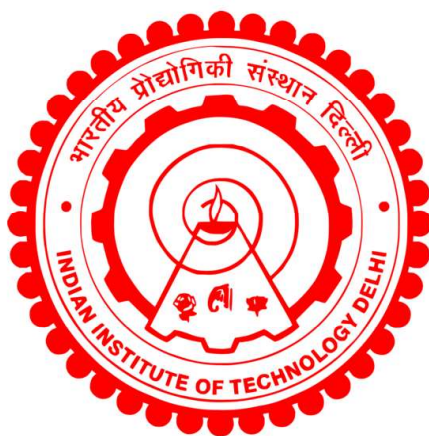


MULTIFUNCTIONAL RESPONSIVE NANOMATERIALS FOR THERANOSTICS AND METAL ION SEQUESTRATION

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**DEPARTMENT OF CHEMISTRY
INDIAN INSTITUTE OF TECHNOLOGY DELHI**

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by

NIKHIL KUMAR

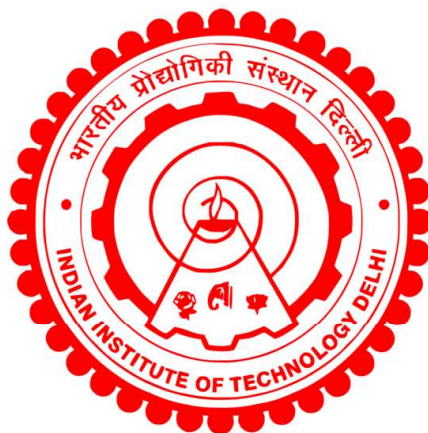
Department of Chemistry

Submitted

In fulfillment of the requirements of the degree of

Doctor of Philosophy

to the



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August 2025

Dedicated to

The guiding star of my life – my mother

and

*In cherished memories of my father & grandparents,
who continue to bless from their heavenly home*

CERTIFICATE

This is to certify that the thesis entitled, “**Multifunctional Responsive Nanomaterials for Theranostics and Metal Ion Sequestration**” being submitted by **Mr. Nikhil Kumar** to the **Indian Institute of Technology Delhi** for the award of the degree of **Doctor of Philosophy in Chemistry**, is an authentic record of research work carried out by him. He has worked under the guidance and supervision of Prof. Jai Deo Singh and Dr. Anupama Datta. The work has not been submitted, in part or in full, to any other university or institute for the award of any degree or diploma. Mr. Nikhil Kumar has fulfilled the requirements for the submission of this thesis, which, to my knowledge has reached the requisite standard.

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न चौरहार्यं न च राजहार्यं न भ्रातृभाज्यं न च भारकारी।

व्यये कृते वर्धत एव नित्यं विद्याधनं सर्वधनप्रधानम्॥

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Nikhil Kumar

ABSTRACT

Nanotechnology has revolutionized biomedical and environmental sciences through the development of multifunctional nanomaterials with applications in theranostics and metal ion sequestration. This thesis explores the synthesis, characterization, and application of nanomaterials designed for multifunctional use in disease diagnosis, treatment, and sequestration of metal ions for environmental remediation. The study focuses on the development of responsive nanomaterials capable of targeted drug delivery, multimodal imaging, and efficient metal ion sequestration. The subject matter of the thesis has been divided into five chapters.

Chapter 1 provides a comprehensive overview of recent advancements in nanomaterials, emphasizing their role in theranostics and environmental applications. Various organic (carbon-based, polymeric, and dendritic) and inorganic (metal, metal oxide, and mesoporous silica) nanomaterials are discussed, highlighting their structural and functional properties that enable selective and efficient biomedical and environmental applications.

Chapter 2 details the development of a nanoapatite loaded injectable cryogel composed of polyvinyl alcohol and κ -carrageenan for hemostasis and wound healing. The cryogel, infused with an antimicrobial drug, promotes rapid blood coagulation and sustained antibacterial effects. The study demonstrates the effectiveness of calcium, magnesium, and phosphate ions in facilitating coagulation factor activation and platelet aggregation, ensuring efficient wound healing.

Chapter 3 presents the synthesis and application of tri-functionalized mesoporous silica nanoparticles for the diagnosis and therapy of prostate cancer. The nanoparticles are functionalized with a choline-derived targeting ligand for selective binding to prostate cancer cells and a chelating agent for ^{99m}Tc labeling, enabling enhanced Single Photon Emission

Computed Tomography imaging. Docetaxel is incorporated within the pores for effective chemotherapy. The results indicate enhanced cellular uptake, improved cytotoxicity, and high imaging contrast, demonstrating the potential of these nanoparticles in targeted prostate cancer theranosis.

Chapter 4 explores the targeted drug delivery and imaging of bone metastases using a bisphosphonate derivative of alanine grafted on mesoporous silica nanocarriers. The nanoparticles are designed for selective accumulation in metastatic bone tissues, with alendronate acting as an osteoporotic drug. SPECT imaging is facilitated by ^{99m}Tc chelation, allowing real-time tracking of drug distribution. The controlled release of alendronate ensures sustained therapeutic efficacy, highlighting the clinical potential of these nanocarriers in theranosis of bone metastasis.

Chapter 5 is a spinoff study of environmental applications by examining the sequestration of uranyl ions using bisphosphonate-functionalized mesoporous silica nanoparticles compared to the amine-functionalized nanoparticles. The synthesized sorbent exhibited high adsorption capacities under various physicochemical conditions, demonstrating their efficiency in metal ion removal. Adsorption isotherm and kinetic studies confirm rapid and selective uranium binding, making it a promising candidate for environmental remediation.

Overall, this research establishes the versatility and effectiveness of multifunctional nanomaterials in theranostics and metal ion sequestration. The findings contribute to the advancement of nanomedicine and environmental science, offering innovative solutions for disease treatment and heavy metal detoxification. Future research will focus on in vivo evaluations, clinical trials, and scalability to enhance the translational potential of these nanomaterials in healthcare and environmental sustainability.

शोध प्रबंध का सार

नैनोटेक्नोलॉजी ने जैव-चिकित्सा और पर्यावरण विज्ञान में क्रांति ला दी है, जिससे थेरेनोस्टिक्स और धातु आयन अवशोषण के लिए बहुक्रियाशील नैनोमैटेरियल्स का विकास संभव हुआ है। यह शोध प्रबंध जैविक और अकार्बनिक नैनोमैटेरियल्स के संश्लेषण, लक्षण-वर्णन और अनुप्रयोगों की खोज करता है, जिन्हें रोगों के निदान, उपचार और पर्यावरणीय सुधार के लिए यूरेनिल आयनों के अवशोषण हेतु डिज़ाइन किया गया है। इस अध्ययन का मुख्य ध्यान उन उत्तरदायी (रेस्पॉन्सिव) नैनोमैटेरियल्स के विकास पर केंद्रित है, जो लक्षित औषधि वितरण, मल्टीमॉडल इमेजिंग और प्रभावी धातु आयन अवशोषण में सक्षम हैं। इस शोध प्रबंध को पाँच अध्यायों में विभाजित किया गया है:

अध्याय 1

इस अध्याय में नैनोमैटेरियल्स में हालिया प्रगति की समग्र समीक्षा दी गई है, जिसमें थेरेनोस्टिक्स और पर्यावरणीय अनुप्रयोगों में उनकी भूमिका को उजागर किया गया है। इसमें विभिन्न जैविक (कार्बन-आधारित, पॉलिमरिक, और डेंड्रिटिक) एवं अकार्बनिक (धातु, धातु ऑक्साइड और मेसोपोरस सिलिका) नैनोमैटेरियल्स पर चर्चा की गई है। इनकी संरचनात्मक और कार्यात्मक विशेषताओं को रेखांकित किया गया है, जो उन्हें चयनात्मक और प्रभावी जैव-चिकित्सा और पर्यावरणीय अनुप्रयोगों के लिए सक्षम बनाती हैं।

अध्याय 2

यह अध्याय हेमॉस्टेसिस और घाव भरने के लिए नैनोअपाटाइट-युक्त इंजेक्टेबल क्रायोजेल के विकास की जांच करता है, जो पॉलीविनाइल अल्कोहल और κ -कैराजेनन से बना है। यह क्रायोजेल एक एंटीमाइक्रोबियल दवा से संचारित है, जो तेज़ रक्त जमने और निरंतर जीवाणु-रोधी प्रभाव को बढ़ावा देता है। अध्ययन से पता चलता है कि कैल्शियम, मैग्नीशियम और फॉस्फेट आयन, कोएगुलेशन फैक्टर

सक्रियण और प्लेटलेट एग्रीगेशन को सुविधाजनक बनाते हैं, जिससे प्रभावी घाव भरने की प्रक्रिया सुनिश्चित होती है।

अध्याय 3

यह अध्याय प्रोस्टेट कैंसर के थेरेनोस्टिक्स के लिए त्रि-कार्यात्मक मेसोपोरस सिलिका नैनोपार्टिकल्स के संश्लेषण और अनुप्रयोग को प्रस्तुत करता है। इन नैनोकणों को कोलाइन-व्युत्पन्न लक्षित लिगेण्ड के साथ कार्यात्मक बनाया गया है, जो प्रोस्टेट कैंसर कोशिकाओं से चयनात्मक रूप से जुड़ता है। साथ ही, इन नैनोपार्टिकल्स को ^{99m}Tc लेबलिंग के लिए एक चिलेटिंग एजेंट से भी जोड़ा गया है, जिससे सिंगल फोटोन एमिशन कंप्यूटेड टोमोग्राफी इमेजिंग में वृद्धि होती है। इसके अलावा, डोसेटैक्सेल को छिद्रों में शामिल किया गया है, जिससे प्रभावी कीमोथेरेपी संभव होती है। परिणाम बताते हैं कि इन नैनोकणों के उपयोग से सेलुलर ग्रहण में वृद्धि, बेहतर साइटोटॉक्सिसिटी और उच्च इमेजिंग कंट्रास्ट प्राप्त हुआ, जिससे यह साबित होता है कि ये नैनोकण लक्षित प्रोस्टेट कैंसर थेरेनोसिस में प्रभावी हो सकते हैं।

अध्याय 4

यह अध्याय मेसोपोरस सिलिका नैनोकैरियर्स पर ग्राफ्टेड एलानाइन डेरिवेटिव बिस्फॉस्फोनेट का उपयोग करके हड्डी में हुए मेटास्टेसिस के लक्षित औषधि वितरण और इमेजिंग की खोज करता है। इन नैनोकणों को मेटास्टेटिक हड्डी ऊतकों में विशेष रूप से जमा होने के लिए डिज़ाइन किया गया है, जिसमें एलेंड्रोनेट एक ऑस्टियोपोरोसिस-रोधी दवा के रूप में कार्य करता है। ^{99m}Tc चिलेशन द्वारा सिंगल फोटोन एमिशन कंप्यूटेड टोमोग्राफी इमेजिंग संभव होती है, जिससे औषधि वितरण का रियल-टाइम में ट्रैकिंग की जा सकती है। नियंत्रित रूप से जारी होने वाला एलेंड्रोनेट निरंतर चिकित्सीय प्रभाव सुनिश्चित करता है, जो हड्डी मेटास्टेसिस के थेरेनोसिस में इन नैनोकैरियर्स की नैदानिक संभावनाओं को उजागर करता है।

अध्याय 5

यह अध्याय पर्यावरणीय अनुप्रयोगों पर केंद्रित है, जिसमें बिस्फॉस्फोनेट-कार्यात्मकित मेसोपोरस सिलिका नैनोकणों द्वारा यूरेनिल आयनों के अवशोषण की तुलना एमाइन-कार्यात्मकित नैनोकणों से की गई है। संश्लेषित सोर्बेंट ने विभिन्न भौतिक-रासायनिक परिस्थितियों के तहत उच्च अवशोषण क्षमता दिखाई, जिससे यह धातु आयन निष्कासन में प्रभावी सिद्ध हुआ। अवशोषण समतुल्य और गतिकी अध्ययन ने तेज़ और चयनात्मक यूरेनियम बाइंडिंग की पुष्टि की, जिससे यह पर्यावरणीय सुधार के लिए एक संभावित उम्मीदवार बन गया।

समग्र रूप से, यह शोध थेरेनोस्टिक्स और धातु आयन अवशोषण में बहुक्रियाशील नैनोमैटेरियल्स की बहुमुखी प्रतिभा और प्रभावशीलता को स्थापित करता है। इस अध्ययन के निष्कर्ष नैनोमेडिसिन और पर्यावरण विज्ञान में प्रगति में योगदान देते हैं और रोग उपचार एवं भारी धातु डिटॉक्सीफिकेशन के लिए नवीन समाधान प्रदान करते हैं। भविष्य के शोध में इन-विवो मूल्यांकन, नैदानिक परीक्षण और इन नैनोमैटेरियल्स की व्यावसायिक उत्पादन क्षमता पर ध्यान केंद्रित किया जाएगा, जिससे इन्हें स्वास्थ्य देखभाल और पर्यावरणीय स्थिरता में प्रभावी रूप से लागू किया जा सके।

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ABBREVIATIONS

AAZTA	6-Amino-6-methylperhydro-1,4-diazepinetetraacetic acid
ALD	Alendronate
APTES	(3-Aminopropyl)triethoxysilane
BBD-RSM	Box–Behnken Design-Response Surface Methodology
BET	Brunauer Emmett Teller
BCI	Blood Clotting Index
CTAB	Cetyltrimethylammonium Bromide
CTL1	Choline Transporter-Like Protein 1
DAPI	4',6-Diamidino-2-phenylindole
DMSO	Dimethyl Sulfoxide
DTPA	Diethylenetriaminepentaacetic Acid
DTX	Docetaxel
EDX	Energy-Dispersive X-ray Spectroscopy
EPR	Enhanced Permeability and Retention
FACS	Fluorescence-Activated Cell Sorting
FDA	Food and Drug Administration
FDG	Fluorodeoxyglucose
FTIR	Fourier Transform Infrared Spectroscopy
GMP	Good Manufacturing Practice
H&E	Hematoxylin and Eosin Staining
HRTEM	High-Resolution Transmission Electron Microscopy
ICP-MS	Inductively Coupled Plasma Mass Spectrometry
ITLC	Instant Thin Layer Chromatography

JCPDS	Joint Committee on Powder Diffraction Standards
LVER	Linear Viscoelastic Region
MSN	Mesoporous Silica Nanoparticles
MTT	3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium Bromide
NMR	Nuclear Magnetic Resonance
PBS	Phosphate-Buffered Saline
PC	Prostate Cancer
PET	Positron Emission Tomography
PGA	Polyglycolic Acid
PI	Propidium Iodide
PVP	Polyvinylpyrrolidone
PXRD	Powder X-ray Diffraction
RANKL	Receptor Activator of Nuclear Factor Kappa-B Ligand
RSM	Response Surface Methodology
SPECT	Single Photon Emission Computed Tomography
TEOS	Tetraethyl Orthosilicate
TEM	Transmission Electron Microscopy
TGA	Thermogravimetric Analysis
TRUS	Transrectal Ultrasound
UV-Vis	Ultraviolet-Visible Spectroscopy
XPS	X-ray Photoelectron Spectroscopy
XRD	X-ray Diffraction