Near Infrared Active Upconversion Nanophosphors for Theranostics, Sensing and Photocatalysis

A thesis

submitted by

Kumbam Lingeshwar Reddy (D12056)

for the award of the degree of

Doctor of Philosophy



School of Basic Sciences

Indian Institute of Technology Mandi

Jun. 2018

Dedicated to Almighty Sri Rama and My Beloved Parents



INDIAN INSTITUTE OF TECHNOLOGY MANDI MANDI- 175 005 (H.P.), INDIA

www.iitmandi.ac.in

Declaration by the Research Scholar

I hereby declare that the entire work embodied in this Thesis is the result of investigations carried out by me in the **School of Basic Sciences**, Indian Institute of Technology Mandi, under the supervision of **Dr. Venkata Krishnan**, and that it has not been submitted elsewhere for any degree or diploma. In keeping with the general practice, due acknowledgements have been made wherever the work described is based on finding of other investigators.

Place: Mandi, Himachal Pradesh, INDIA

Date: Feb. 13, 2018

Signature:

Name: Kumbam Lingeshwar Reddy

Declaration by the Research Advisor

I hereby certify that the entire work in this Thesis has been carried out by **Mr. Kumbam Lingeshwar Reddy,** under my supervision in the **School of Basic Sciences**, Indian Institute of Technology Mandi, and that no part of it has been submitted elsewhere for any Degree or Diploma.

Place: Mandi, Himachal Pradesh, INDIA

Date: Feb. 13, 2018

Signature:

Name: Dr. Venkata Krishnan

Verkata Knishman

Acknowledgements

During my journey towards Ph.D. degree, lot of graceful hearts fortified me towards right direction and enlightened me with their knowledge and experience. I will always be thankful to them.

First and foremost, I would like to thank my Ph.D. advisor Dr. Venkata Krishnan for his valuable suggestions and rectification of my silly errors, which enabled me to achieve the task of undertaking the research. He sets an example of a world-class researcher by his passion for research. His immense knowledge and logical way of thinking have been of great value for me. His understanding, encouragement and personal guidance provided a base not only for my Ph.D. thesis, but also for me to groom as a good human being.

I express my sincere thanks to the Director, IIT Mandi for his support and encouragement. The research facility at Advanced Materials Research Center (AMRC), IIT Mandi and in other departments also gratefully acknowledged hereby.

My sincere thanks to all the faculty members in IIT Mandi for their invaluable advice and encouragement during course work as well as in research work. I express my special thanks to Dr. Abhimanew Dhir, his wisdom towards grooming researchers is quite unique and it enlightened my knowledge in understanding complex topics.

I would like to thank my doctoral committee members Dr. Prasanth P. Jose, Dr. Abhimanew Dhir, Dr. Pradeep Parameswaran and Dr. Satinder Sharma for their precious support and motivation throughout my stay at IIT Mandi. I have significantly benefitted by their recommendations regarding the plan of studies and approaches for research work.

I am also very much thankful to my research group members: Vipul, Suneel, Ashish, Balaji, Ravi, Ashish, Ajay, Tripti, Nisha, Diksha, Harpreet and all graduate students for their valuable support and help during my research work. I would also like to extend my sincere thanks to Manoj, Srinivas and Nikhil, who worked with me and helped a lot in successfully completing my research tasks. I have learnt many things from all the groupmates during my stay at IIT Mandi, due to which it was possible for me to complete everything in time.

I would also like to thank Dr. Satyanarayana, Dr. Rajesh, Abhinay, Rambabu, Venkateswarulu, Prateep, Nagaraju, Guruprasad, Krishnakanth, Rajkumar and several other friends at IIT Mandi for their continuous support and encouragement. My earnest thanks are due to AMRC staff and IIT Mandi office staffs for their assistance in and outside the lab.

I would also like to express my special thanks to our collaborator, Dr. Jessica Rosenholm, for allowing me to work with her by accommodating me in her research group in Abo Akademi University, Finland. I would also like to acknowledge Neeraj, Dr. Eudald, Dr. Riikka, Dr. Diti, Dr. Motolani, Dr. Parthiban and Vipin for their help during my stay at Abo Akademi University, Finland.

I would also like to express my gratitude to all our collaborators, Dr. Abhimanew Dhir, Dr. Neha Garg, Dr. Subrata Ghosh from IIT Mandi, Dr. Suneel Kumar Singh from IIT BHU, Dr. Shyam Bahadur Rai from BHU, Dr. Yashveer Singh from IIT Ropar and Dr. Kaustava Bhattacharya from BARC. I would also like to thank Dr. Monika Rai, Peeyush and Ashutosh for their support to accomplish my research tasks.

I would like to acknowledge Ministry of Human Resource Development (MHRD), Government of India for the doctoral scholarship and other miscellaneous financial support.

I would also like to acknowledge financial support from Center for International Mobility (CIMO), Finland for the visit to Abo Akademi University, Finland.

I would like to express my special words of gratitude to my beloved brother Lukesh, sister-in-law, Shilpa for their continuous inspiration, motivation and cooperation. I express profound sense of reverence to my parents for their untiring support and cooperation. I can never forget cooperation, endless tolerance and constant encouragement from all my family members during the tough and happy moments of the journey.

Above all, all the praise is due to the Almighty Sri Rama, the ultimate source of knowledge, a part of which he reveals to man, and peace be upon all his messengers throughout the world for success and guidance of mankind. I express my gratitude and indebtedness to the Almighty for countless blessings.

Abbreviations

α-CD	α-Cyclodextrin
ACN	Acetonitrile
AcOH	Acetic acid
BET	Brunauer-Emmett-Teller
CCM	Curcumin
Cys	Cysteine
DD	Drug delivery
DLS	Dynamic light scattering
DOX	Doxorubicin
EDAX	Energy-dispersive X-ray analysis
EtOH	Ethanol
FESEM	Field emission scanning electron microscopy
Glu	Glutathione
Hcy	Homocysteine
HRTEMHi	gh resolution transmission electron microscopy
MDR	Multi-drug resistance
MB	Methylene blue
mSiO ₂	Mesoporous silica
NIR	Near infrared
OA	Oleic acid
PEG	Polyethylene glycol
PBS	Phosphate buffer solution
PDT	Photodynamic therapy
PEI	Polyethylene imine
ReAc	Resorufin acrylate
RePr	Resorufin propionate
ROS	Reactive oxygen species
SAED	Selected-area electron diffraction
SPR	Surface plasmon resonance

UCL	Upconversion luminescence
UCNC	Upconversion nanocrystals
UCNP	Upconversion nanoparticles
UV	Ultra violet
Vis	Visible
XRD	X-ray diffraction
XPS	X-ray photoelectron spectroscopy

Table of Contents

Chapter 1. Introduction	1
1.1. Importance of the work	2
1.2. Aims and objectives	2
1.3. References	3
Chapter 2. Literature Review	6
Abstract	7
2.1. Introduction	7
2.2. Fundamental concepts	9
2.2.1. Host, activator and sensitizer for Lanthanide-doped UCNP	9
2.3. Upconversion luminescence mechanisms	11
2.3.1. Excited state absorption	12
2.3.2. Energy transfer upconversion	13
2.3.3. Cooperative sensitization upconversion	13
2.3.4. Cross relaxation	14
2.3.5. Photon avalanche	14
2.3.6. Energy migration-mediated upconversion	14
2.4. Synthesis strategies	15
2.4.1. Thermal decomposition	15
2.4.2. Co-precipitation method	16
2.4.3. Solvo/hydrothermal synthesis	17
2.4.4. Sol-gel method	18
2.4.5. Microemulsion	19
2.4.6. Combustion	20
2.4.7. Flaming synthesis	21
2.4.8. Electrospinning	22
2.4.9. Microwave synthesis	23
2.4.10. Mechanochemical preparation	24
2.5. Upconversion nanophosphors for biomedical applications	24

	2.5.1. Bioimaging	25
	2.5.2. Drug delivery	29
2.6. l	Upconversion nanophosphors for sensing applications	33
2.7. l	Upconversion nanophosphors for photocatalysis applications	37
2.8. l	Upconversion nanophosphors for other technological applications	43
2.9. 0	Conclusion	49
2.10.	. References	49
Chap	oter 3. Materials and Methods	80
3.1. [Materials	81
3.2. 9	Synthesis procedures	82
	3.2.1. Synthesis of Mn ²⁺ doped NaYF ₄ :Yb/Ho nanoparticles	82
	3.2.2. PEG-PEI co-polymer synthesis and functionalization of UCNP	82
,	3.2.3. Synthesis of NaYF ₄ :Yb/Ho/Mn by varying the reaction time	83
	3.2.4. Synthesis of NaYF ₄ :Yb/Ho/Mn by varying the solvent (ET/OA) ratio	83
	3.2.5. Synthesis of NaYF ₄ :Yb/Ho/Mn by varying the reaction temperature	83
	3.2.6. Synthesis of NaYF ₄ :Yb/Ho/Mn at optimized reaction conditions	83
	3.2.7. Microwave assisted synthesis of NaYF ₄ :Yb/Er nanophosphors	84
	3.2.8. UCNC@SiO $_2$ core-shell nanostructures	84
	3.2.9. Synthesis of hexagonal NaYF ₄ :Yb/Er nanophosphors	84
	3.2.10. Porous silica-coated NaYF ₄ :Yb/Er (UCNP@mSiO ₂)	85
	3.2.11. Synthesis of resorufin propionate	85
	3.2.12. Synthesis of OA stabilized NaYF ₄ :Yb/Er	86
	3.2.13. Synthesis of α -CD modified UCNP	86
	3.2.14. Assembly of RePr onto the surface of α -CD modified UCNP (RePr-UCNP)	86
	3.2.15. Synthesis of resorufin acrylate (ReAc)	87
	3.2.16. Synthesis of Ag-Cu bimetallic nanoparticles	87
	3.2.17. Synthesis of active-core NaYF ₄ :Yb/Tm@ active-shell NaYF ₄ :Yb	
	upconversion phosphors (UCP)	88
	3.2.18. Synthesis of UCP@TiO ₂ core-porous shell microstructures (UCPT)	88
	3.2.19. Ag-Cu nanoparticles decorated UCP@TiO ₂ core@porous shell	
	microstructures	89

3.3. Instrumentation	89
3.3.1. Microwave synthesizer	89
3.3.2. X-ray diffraction (XRD)	89
3.3.3. X-ray photoelectron spectroscopy (XPS)	89
3.3.4. Transmission electron microscopy (TEM)	90
3.3.5. Field Emission scanning electron microscopy (FESEM)	90
3.3.6. UV-vis spectroscopy	90
3.3.7. UV-vis-NIR diffuse reflectance spectroscopy	91
3.3.8. Fluorescence spectrometer	91
3.3.9. Inverted microscope	91
3.3.10. Multiphoton (MP) microscope	91
3.3.11. Digital camera	91
3.3.12. Nuclear magnetic resonance (NMR) spectroscopy	92
3.3.13. High resolution mass spectrometry (HRMS)	92
3.3.14. Fourier-transform infrared spectroscopy (FTIR)	92
3.3.15. Brunauer-Emmett-Teller (BET) surface area and pore volume analyzer	92
3.3.16. Solar simulator	92
3.3.17. UV illumination chamber	92
3.3.18. Centrifugation	93
3.3.19. Zetasizer	93
3.4. Cell culture and viability	93
3.5. Bioimaging experiments	94
3.6. Cell uptake studies	94
3.7. In vitro drug loading and release studies	94
3.8. Analysis of hydrazine in environmental samples	95
3.9. Analysis of biothiols in blood serum	96
3.10. Photocatalysis experiments	96
3.11. References	97
Chapter 4. Upconversion Nanophosphors for Theranostics	99
Abstract	100
4.1. Upconversion nanophosphors prepared using solvothermal method	102

4.1.1. Influence of Mn doping	102
4.1.2. Influence of reaction parameters	110
4.2. Upconversion nanophosphors prepared using microwave assisted method	127
4.2.1. Acetate-capped upconversion nanocrystals	128
4.2.2. Silica-coated upconversion nanocrystals	136
4.3. Upconversion nanophosphors for drug delivery	143
4.4. References	153
Chapter 5. Upconversion Nanophosphors for Sensing and Photocatalysis	159
Abstract	160
5.1. Upconversion nanophosphors for detection of hydrazine in environmental	
samples	161
5.2. Upconversion nanophosphors for detection of biothiols in blood serum	177
5.3. Upconversion nanophosphors for photocatalytic environmental remediation	185
5.4. References	198
	202
Chapter 6. Summary and Future Perspectives	
6.1. Summary	203
6.2. Future perspectives	204
List of publications	206