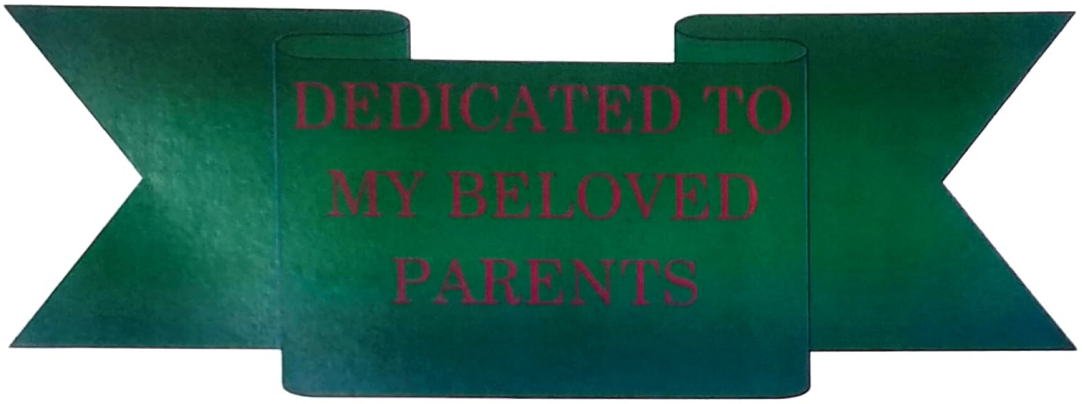
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CERTIFICATE

This is to certify that thesis entitled **"Polymeric nanoparticle for the delivery of poorly soluble drugs"** submitted by **Ms. Kushagri Singh** in fulfillment of requirement for the award of the degree of Doctor of Philosophy at the School of Biochemical Engineering, Indian Institute of Technology (Banaras Hindu University), Varanasi, is a record of bonafide work carried out by her under my supervision for the prescribed period in conformity with the rules and regulations of the Ph.D ordinances of the Indian Institute of Technology (Banaras Hindu University). This thesis embodies the results of her investigations conducted during this work as a Ph.D research Scholar.

18.5.18

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UNDERTAKING BY THE CANDIDATE

I, **Kushagri Singh**, declare that the work embodied in this Ph.D thesis is my own bonafide work carried out under the supervision of **Dr. Abha Mishra** for a period of **5 years and 8 months** from **September 2012 to May 2018** at the School of Biochemical Engineering, 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.

Though care has been taken while writing this thesis, there may still be some errors (typographical or otherwise) which are inadvertent on my part.

Date: 18.05.18

Place: IIT (BHU), Varanasi

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DECLARATION BY THE CANDIDATE

I, **Kushagri Singh**, certify that the work embodied in this Ph.D thesis is my own bonafide work carried out by me under the supervision of **Dr. Abha Mishra** for a period of **5 years and 8 months** from **September 2012 to May 2018** at the School of Biochemical Engineering, 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 and referred to the research workers wherever their works have been cited in the text and the body of the thesis. I further certify that I have not willfully lifted up some other's work, paragraph, text, data, results, etc. reported in the journals, books, magazines, reports, dissertations, thesis, etc., or available at websites and included in this Ph.D thesis and cited as my own work.

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CERTIFICATE FROM THE SUPERVISOR

This is to certify that the above statement made by the candidate is correct to the best of our knowledge.

18/05/2018

Signature of the Coordinator
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is is to certify that **Ms. Kushagri Singh**, a bonafide research scholar of School of ochemical Engineering, has satisfactorily completed the course work/comprehensive amination/candidacy/state of art requirement, which is a part of her Ph.D program.

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I bow my head with great reverence in the pious feet to the founder of this University, Late ***Mahamana Pandit Madan Mohan Malviya*** *a man of great vision for creating such a wonderful and unique University, a temple of learning for thousands of students like me.*

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Date: 18.05.18

Place: Varanasi

Kushagri Singh

(Kushagri Singh)

TABLE OF CONTENTS

LIST OF ABBREVIATIONS & SYMBOLS

CS	CHITOSAN
CSNP	CHITOSAN NANOPARTICLES
TCS	THIOLATED CHITOSAN
SEM	SCANNING ELECTRON MICROSCOPY
TEM	TRANSMISSION ELECTRON MICROSCOPY
TPP	TRIPOLYPHOSPHATE
EDTA	ETHYLENEDIAMINETETRAACETICACID
DDA	DEGREE OF DEACETYLATION
DDS	DRUG DELIVERY SYSTEM
FTIR	FOURIER TRANSFORM INFRARED
EE	ENTRAPMENT EFFICIENCY
LC	LOADING CAPACITY
XRD	X-RAY DIFFRACTION
NPS	NANOPARTICLES
PDI	POLYDISPERSITY INDEX
NDDS	NOVEL DRUG DELIVERY SYSTEM
H	HOURS
MINS	MINUTES
MG	MILIGRAMS
ML	MILILETER
ZP	ZETA-POTENTIAL
NM	NANO-METER
API	ACTIVE PHARMACEUTICAL INGREDIENT

M	METER
µM	MICROMETER
Da	DALTON
AmB	AMPHOTERICIN B
VCM	VANCOMYCIN
BCS	BIOPHARMACEUTICAL CLASSIFICATION SYSTEM
AE	ADVERSE EFFECTS
SD	STANDARD DEVIATION
NA	NUTRIENT AGAR
PDA	POTATO DEXTROSE AGAR
R^2	CORRELATION COEFFICIENT
TLA	THIOLACTIC ACID
EDC	ETHYL DIMETHYLAMINOPROPYL CARBODIIMIDE
KBr	POTASSIUM BROMIDE
PBS	PHOSPHATE BUFFER SOLUTION

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PREFACE

Effective delivery of active pharmaceutical ingredient or drug has become a major challenge to pharmaceutical industry today. This problem is mainly because of poor solubility of drugs and around 40% of the oral marketed drugs have low bioavailability. Due to rising number of compounds having solubility and permeability issues, finding ways to enhance the solubility of drugs is one of the major concern in the pharmaceutical industry today. Drug absorption, sufficient bioavailability and pharmacokinetic profile of oral drugs are highly dependent on solubility of that compound in aqueous medium. Solubility is one of the important parameters to achieve preferred concentration of drug in systemic circulation for achieving required pharmacological response. Poorly soluble oral drugs having slow drug absorption that leads to gastrointestinal mucosal toxicity, variable bioavailability and undesirable side effects. The solubility behavior of poorly soluble oral drugs remains one of the most challenging aspects of formulation development. Use of nanotechnology in delivery of poorly soluble oral drugs especially antimicrobial agents could improve the bioavailability together with sustained delivery. Numerous advanced functional materials have been investigated.

Among them, nano-carriers strategies have been widely used to enhance the dissolution and oral availability of poorly soluble drugs by encapsulating the drugs into nano-carriers and changing the crystalline form into amorphous together with protection of drugs from enzymatic as well as chemical degradation. Polymeric nanoparticles possess many advantages over conventional and some novel dosage forms such as non-toxicity, biodegradability, stability, sustained delivery of drugs and reproducibility. Polymeric chitosan nanoparticles formulated and loaded with five different antimicrobial agents such as Amphotericin B, Ketoconazole, Ciprfloxacin, Vancomycin and Chloramphenicol. These drug loaded chitosan nanoparticle fromulations were then characterized on the basis of different factors and a comparative study was done to check the release status of drug from chitosan nanoparticles, thiolated chitosan nanoparticles and release of free drug itself.

This thesis comprise of mainly five chapters namely Introduction, Review of Literature, Material and Methods, Results and Discussion, and Conclusion. From the discussions on the results that we obtained I believe that it is possible for one to get a better understanding of stable formulation development of chitosan and thiolated chitosan nanoparticles loaded with poorly soluble oral antimicrobial drugs to increase its dissolution as well as absorption through GI tract. This research attempts to develop polymeric chitosan nanoparticles to meet the needs that are required for a successful nano delivery system for poorly soluble oral antimicrobial agents.