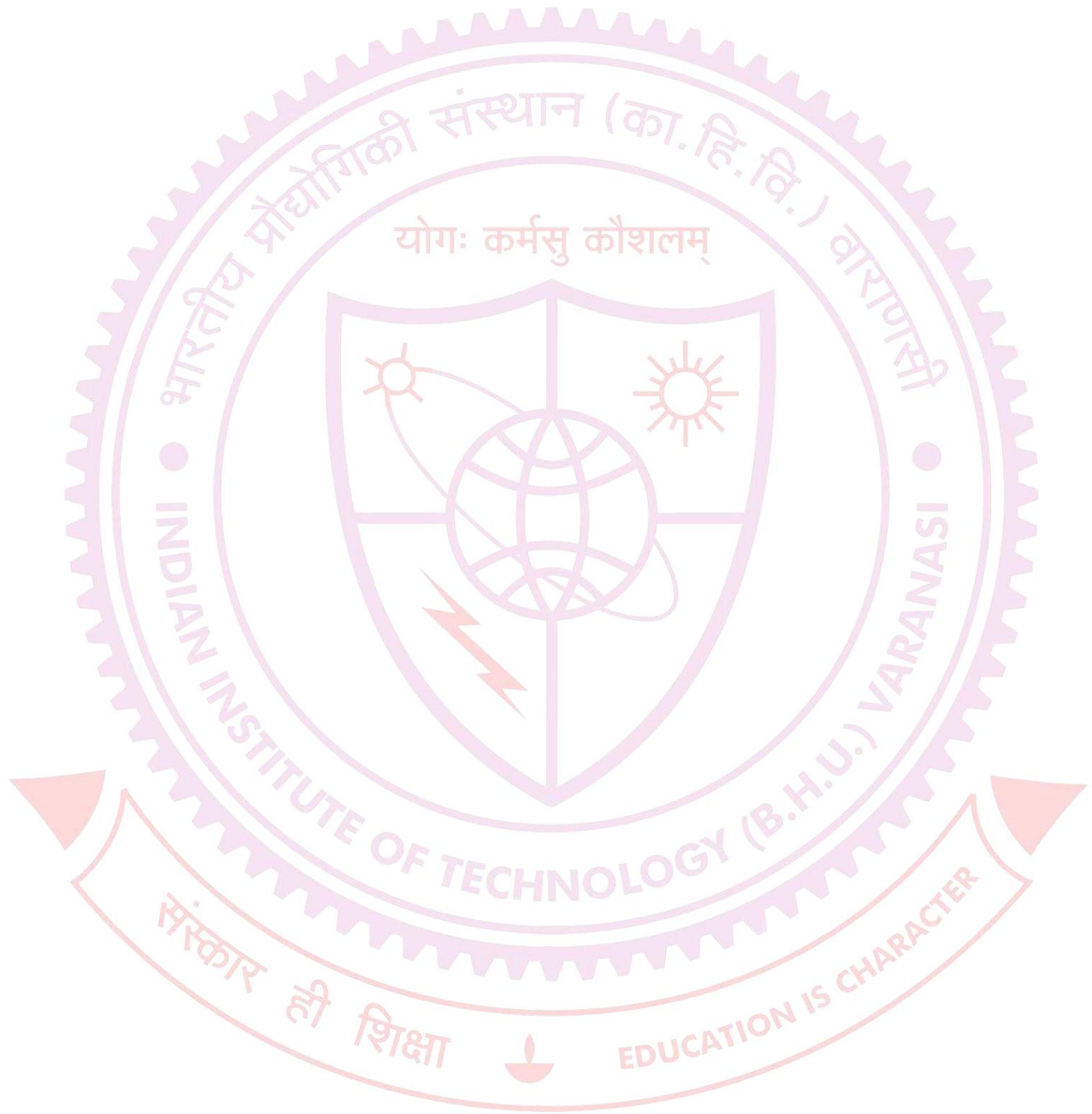


*Dedicated to my
Beloved Parents*



**Copyright © Indian Institute of Technology,
(Banaras Hindu University), Varanasi, INDIA, 2014.
All rights reserved.**

UNDERTAKING BY THE CANDIDATE

I, **Mr. Nirupam Das**, declare that I have pursued my research work under the supervision of **Prof. Sushant Kumar Shrivastava** from July 2008 to October 2014. I am hereby submitting my thesis entitled “**Design, synthesis, pharmacological evaluation and molecular modelling study of quinazolin-4(3*H*)-ones as potential anticonvulsant agents**” for the award of the Ph.D. degree.

Date:

Place: IIT (BHU), Varanasi

(Mr. Nirupam Das)

ANNEXURE-E

CANDIDATE'S DECLARATION

I, **Mr. Nirupam Das**, certify that the work embodied in this Ph.D. thesis is my own bonafide work carried out by me under the supervision of **Prof. Sushant Kumar Shrivastava** for a period of about **6 years and 3 months** from **July, 2008** to **October, 2014** at **Department of Pharmaceutics, Indian Institute of Technology (Banaras Hindu University), Varanasi**. The matter embodied in this Ph.D. 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, para, text, data, results etc. reported in the journals, books, magazines, reports, dissertations, theses, etc., or available at websites and included them in this Ph.D. thesis and cited as my own work.

Date:

Place: IIT (BHU), Varanasi

(Mr. Nirupam Das)

Certificate from the Supervisor and Head of the Department

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

Supervisor Signature
Dr. S. K. Shrivastava
Professor

(Signature of the Head of the Department with Seal)

ANNEXURE-F

COURSE WORK/COMPREHENSIVE EXAMINATION

COMPLETION CERTIFICATE

This is to certify that **Mr. Nirupam Das**, a bonafide research scholar (Pharmaceutical Chemistry) of this Department, has successfully completed the course work/comprehensive examination requirement, which is a part of his Ph.D. programme.

Date:

Place: IIT (BHU), Varanasi

(Head of the Department)

ANNEXURE-F

PRE-SUBMISSION SEMINAR COMPLETION CERTIFICATE

This is to certify that, **Mr. Nirupam Das**, a bonafide research scholar (Pharmaceutical Chemistry) of this Department, has successfully completed the pre-submission seminar requirement on the topic “**Design, synthesis, pharmacological evaluation and molecular modelling study of quinazolin-4(3H)-ones as potential anticonvulsant agents**” on **31/05/2014**, which is a part of his Ph.D. programme.

Date:

Place: IIT (BHU), Varanasi

(Head of the Department)

ANNEXURE-G

COPYRIGHT TRANSFER CERTIFICATE

Title of the Thesis : “Design, synthesis, pharmacological evaluation and molecular modelling study of quinazolin-4(3*H*)-ones as potential anticonvulsant agents”

Candidate’s Name : Mr. Nirupam Das

Copyright Transfer

The undersigned hereby assigns to the Indian Institute of Technology (Banaras Hindu University), Varanasi all rights under copyright that may exist in and for the above thesis submitted for the award of the Ph.D. degree.

Date:

(Signature of the candidate)

Note: However, the author may reproduce or authorize others to reproduce material extracted verbatim from the thesis or derivative of the thesis for author’s personal use provided that the source and University’s copyright notice are indicated.

Acknowledgements



Foremost, I would like to pay my tribute to the founder of the Banaras Hindu University, **Pandit Madan Mohan Malaviyaji** whose thoughts and values encourage students to give their best and contribute to the nation building. I am very thankful and proud of the education I received at the Banaras Hindu University.

I would like to express my heartfelt gratitude to my revered supervisor, **Prof. Sushant Kumar Shrivastava** for his continuous support during my Ph.D. study and research, for his patience, motivation, and immense knowledge. His guidance helped me during the time of research and writing of this thesis. Without his supervision and constant help this dissertation would not have been possible.

I am also grateful to **Prof. B. Mishra**, Head, Department of Pharmaceutics, Indian Institute of Technology (Banaras Hindu University) and **Prof. R.S. Srivastava**, (Former Head) for allowing me to use the Departmental facilities for carrying out my research work.

I owe my gratitude to all my respected RPC members **Prof. P.V. Sharma, Prof. R.S. Srivastava, Prof. S.K. Srivastava** (Biochemical Engineering, IIT, BHU) and **Prof. S. K. Singh** for their encouragement and insightful comments leading me to the completion of the research work. I would also like to thank all the teachers **Prof. J.K. Pandit, Prof. P. N. Singh, Prof. Sanjay Singh, Dr. (Mrs.) S. Hemlatha, Dr. K. Sairam, Mr. A. K. Srivastava, Dr. Vikas Kumar, Dr. Senthil Raja, Mr. A. N Sahu, Dr. S. K. Mishra, Mrs. Ruchi Chawla,** and **Dr. Ashok Maurya**.

I take the opportunity to sincerely acknowledge the University Grants Commission, Government of India, New Delhi for providing financial support in the form of Junior Research Fellowship and Senior Research Fellowship (Rajiv Gandhi National Fellowship), that immensely helped me to achieve my goals. I also thank the Indian Council of Medical Research, New Delhi and Banaras Hindu University for awarding me travel grant to attend an international conference.

I am grateful to the Head, Department of Chemistry, Faculty of Science, Banaras Hindu University, Varanasi, India for ^1H NMR and SAIF–Central Drug Research Institute, Lucknow, India for ^{13}C NMR and Mass analysis.

My sincere thanks to **Dr. Sairam Krishnamurthy** for providing me assistance and required facilities to carry out the pharmacological evaluation. I am also thankful to **Mr. Debapriya Garabadu** and **Mr. Milind Geed** for assisting me in carrying out the animal experiments.

I warmly thank **Mr. Shome Shankar Bhunia** (CDRI, Lucknow) and **Dr. Ravi Kumar Muttineni** (Application Scientist at Schrödinger, Bangalore) for their assistance in carrying out the molecular modelling studies.

I pay my sincere thanks to (late) **Mr. Ajay Pal ji**, **Mr. Nandlal ji**, **Mr. Madan ji**, **Mr. Upadhya ji**, **Mr. Sanjeev ji**, **Mr. Jaamil ji**, **Mr. Pathak ji**, **Mr. Rafeeq ji**, **Mr. Kapil ji**, **Mr. Virendra ji**, **Mr. Chotelal ji**, **Mr. Arun ji**, **Mr. Gopal ji**, **Mrs. Saroj Kumari ji**, **Mrs. Archana Singh ji**, **Mrs. Shyamli Ghoshal ji** and all other non-teaching staff of the Department for their assistance and co-operation during the Ph.D. tenure.

I would particularly like to acknowledge the contribution of **Mr. Anupam G. Banerjee** and it is not sufficient to express my gratitude with only a few words. He has always been there to motivate me during the hour of hardship and helped me unconditionally throughout the tenure.

I am indeed thankful to have got welcoming and friendly fellow mates **Mr. Anupam** and **Dr. Meenakshi** who were ever ready to provide me with all possible help and they created a happy working environment and foster camaraderie within the laboratory. Amongst the juniors, I would like to thank **Biswajit** and **Akanksha** for their alacrity and support during the tenure.

I also acknowledge the warm support extended to me by **Gireesh, Gulam, Ravi Bhushan, Jugal, Achint, Rahul, Sanjay, Saurabh and Damiki**. They made my stay at Varanasi a very pleasant and memorable one. I would also like to express my thanks to my supportive seniors, juniors and fellow research scholars: **Dr. Prabhat Shrivastava, Dr. Sanjay Bharti, Dr. Monoj Rawat, Dr. Shailendra Pandey, Dr. Dinesh Patel, Dilip, Pramila, Madhu, Dr. Sanjay Tiwari, Manish Kumar, Anshul, Gopal, Pavan, Prabhash and Nagendra** to name a few and all the Research Scholars of the Department who were always there with a helping attitude whenever I was in need.

I am also grateful to the Assam University Silchar and to my good colleagues for extending support whenever required. My heartfelt thanks to all my teachers right from school until now for their keen interest, constant encouragement and wishes for my career.

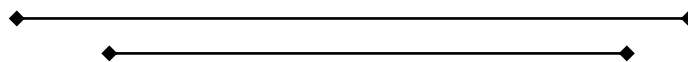
I must express my gratitude to **Sanghita**, my wife, for her emotional support and constant encouragement. A loving appreciation is reserved for my younger brothers, **Pritam** and **Bishwarup**. Most importantly, none of this would have been possible without the love and patience of my family. My parents to whom this thesis is dedicated to, has been a constant source of love, moral support and strength all these years. I owe my achievement to both of them.

Last but not the least, I pray God for the animals who were mortified for the cause of research and advancement of knowledge. I wish for their soul to rest in peace.

Date:

Place: Varanasi

(**Nirupam Das**)



LIST OF ABBREVIATIONS AND SYMBOLS

ILAE – International League Against Epilepsy	ALP – Alanine aminotransferase
GABA – Gamma-aminobutyric acid	AST – Aspartate aminotransferase
ED₅₀ – Median effective dose	SD – Standard deviation
TD₅₀ – Median toxic dose	°C – Degree centigrade
PI – Protective index	μmol – Micromolar
AMPA – α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid	min – Minutes
NMDA – N-methyl-D-aspartate	S – Seconds
iGluRs – Ionotropic receptors	% – Percentage
MES – Maximal electroshock	G score – Glide score
scPTZ – Subcutaneous pentylenetetrazole	m.p. – Melting point
PDB – Protein data bank	μl – Microliter
OECD – Organization for Economic Co-operation and Development	mL – Milliliter
i.p. – Intraperitoneal	mg – Milligram
TLC – Thin layer Chromatography	Kg – Kilogram
FDA – Food and Drug Administration	g – Gram(s)
PEG – Poly(ethylene glycol)	h – Hour
cm – Centimeter	TMS – Tetramethylsilane
FTIR – Fourier transform infrared spectroscopy	NMR – Nuclear Magnetic Resonance
i.c.v – Intracerebroventricular	R_f – Retention factor
OPLS – Optimized Potentials for Liquid Simulations	rpm – Revolution per minute
CDCl₃ – Deuterated chloroform	ATD – Amino terminal domain
CNS – Central nervous system	PNT – Phenytoin
UV – Ultra violet	TLP – Talampanel
Ac₂O – Acetic anhydride	ANOVA – Analysis of variance
	ARG – Arginine
	LYS – Lysine
	SER – Serine
	GYKI 52466 – 1-(4-Aminophenyl)-4-methyl-7,8-methylenedioxy-5H-2,3-benzodiazepine