Studies on Anti-Leishmanial Compound Discovery

Thesis submitted in partial fulfilment for the

Award of Degree

Doctor of Philosophy

by

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I, **Naveena Menpadi**, certify that the work embodied in this thesis is my own bona fide work and was carried out by me under the supervision of **Prof. Vikash Kumar Dubey** and **Dr. Pranjal Chandra** from **July 2019 to July 2025**, at the School of Biochemical Engineering, Indian Institute of Technology (BHU) 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 and 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 willfully copied any other's work, paragraphs, text, data, results, etc., reported in journals, books, magazines, reports, dissertations, thesis, etc., or available at websites and have not included them in this thesis and have not cited them as my own work.

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Dedicated to my parents, family, friends,

and all my mentors……

Acknowledgement

As I draw near the end of this enthralling journey of obtaining my PhD degree, I want to express my gratitude and heartfelt thanks to all the people who have helped me accomplish this journey.

I would like to express my sincere gratitude to my supervisor, ***Prof. Vikash Kumar Dubey,*** and Co-supervisor ***Dr. Pranjal Chandra***, for their constant guidance, encouragement, and motivation. They have always been a source of motivation and inspiration with their wise words and a strong sense of belief. They never failed to instil a strong sense of work ethic in me throughout my journey during various phases of my research and helped me put a conclusion to my work as well. Further, I would like to thank members of RPEC, ***Dr. Prodyut Dhar*** and ***Prof. Rajesh Kumar Upadhyaya***, for their insights into my work and their efforts to increase the overall quality of my work outputs.

I also acknowledge the help of ***Prof. (Dr.) Shyam Sundar*** and ***Dr. Rajiv Kumar*****,** from **IMS, BHU,** for providing *Leishmania* strains for the studies and various help at different stages.

I have been surrounded by some wonderful seniors, batchmates, and juniors throughout my PhD journey. I would like to especially thank ***Dr. Jay Prakash***, ***Dr. Debanjan Kundu***, ***and Dr. Kumari Prerna,*** who played an instrumental role during the preliminary days of my PhD journey. Further, I would like to thank my lab mates, ***Mr. Kushal Bora, Mr. Shiv Kalia, Miss. Atreyee Chatterjee, and Miss. Ankita Mondal*** for their constant support and vigour during our stay together in the Cellular Biochemistry Laboratory. The acknowledgement would be incomplete without mentioning other juniors who completed their IDD and M.Tech. projects from our lab. ***Ria Sonigra, Kshitij Sinha, Neeraj Mauthiya, Saumya Mathur, Shreyan Dutta, Dev Gupta, Yashwant Kumar Naik, Tanuj Handa, Abhishek Sahu, Sneha Kataria and Anurag Kumar Pandey***, all of whom gave me enough opportunities to sharpen my mentoring skills with all the help and assistance they asked for from time to time. I owe special thanks to

our postdoctoral fellow, ***Dr. Ehasanullah Khan***, for his constant support during times when I needed him the most. During one of the critical phases of our research journey, the COVID-19 pandemic, ***Dr. Subhomoi Borkotoky*** emerged as one of our most considerable helpers, whose substantial contribution to my computational biology studies will always stay with me.

I would also like to thank the Ministry of Education, IIT(BHU), and various facilities of the Institute like Central Instrumentation Facility (CIF), CDC-SATHI (BHU) and the Param Shivay Supercomputing, etc.

Lastly, I would like to thank my ever-supportive and loving parents, ***Mrs. A. Vijayalakshmi***, ***Mr. S. Venkataramana*** and my brother, ***Mr. Manoj Menpadi***, without whose blessings and support I would not have been able to complete my journey. The former Coordinators of my School, ***Prof. Pradeep Srivastava*** *and* ***Prof. S. K. Srivastava***, and my M.Tech. Supervisor ***Prof. Mira Debnath Das***, who were always there to support me and provide me with any help whenever required. Last but not the least, I also thank faculty members and all the support staff of my School for their invaluable help and input.

Naveena Menpadi
August 2025

List of Abbreviations

NTD	:	Neglected Tropical Diseases
VL	:	Visceral leishmaniasis
CoA	:	Coenzyme A
DPCK	:	Dephospho-Coenzyme A Kinase
TLR	:	Toll-like receptors
Th	:	Helper T cells
GP	:	Glycoprotein
IL	:	Interleukin
WHO	:	World Health Organisation
IC_{50}	:	Half maximal Inhibitory Concentration
ATP	:	Adenosine Triphosphate
TCA	:	Tricarboxylic Acid
ROS	:	Reactive Oxygen Species
AO	:	Acridine Orange
ATG	:	Autophagy-related genes
RT-qPCR	:	Reverse Transcription-Quantitative Polymerase Chain Reaction
SEM	:	Scanning Electron Microscope
ABC transporters	:	ATP-binding cassette transporters
DNA	:	Deoxyribonucleic Acid
PanK	:	pantothenate kinase
PPCS	:	4' -phosphopantothenoylcysteine synthase
PPCDC	:	4' -phosphopantothenoylcysteine decarboxylase
PPAT	:	4' -phosphoadenylyltransferase
COASY	:	CoA synthase
RNA	:	Ribonucleic acid

PKAN	:	pantothenate kinase-associated neurodegeneration
CoPAN	:	COASY protein-associated neurodegeneration
DCoA	:	Dephospho-Coenzyme A
NTP	:	nucleoside triphosphate
MM-PBSA	:	Molecular Mechanics Poisson-Boltzmann Surface Area
MTT	:	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
µM	:	Micro-molar
mM	:	Milli-molar
CDD	:	Computer-aided Drug Discovery
SVS	:	Structure-based Virtual Screening
LdDPCK	:	*Leishmania donovani* Dephospho-coenzyme A kinase
BLAST	:	Basic Local Alignment Search Tool
GPFs	:	Grid Parameter Files
AMBER	:	Assisted Model Building with Energy Refinement
ADME	:	adsorption, distribution, metabolism and excretion
MD Simulations	:	Molecular Dynamic Simulations
GROMACS	:	GROningen MAchine for Chemical Simulations
SASA	:	Solvent Accessible Surface Area
CO_2	:	Carbon Dioxide
DMSO	:	Dimethyl sulfoxide
CC_{50}	:	Half maximal Cytotoxic Concentration
SI	:	selectivity index
TPSA	:	Topological Polar Surface Area
RMSD	:	root-mean-square deviation
RMSF	:	root-mean-square fluctuation
Rg	:	radius of gyration
Ala	:	Alanine

Arg	:	Arginine
Asn	:	Asparagine
Asp	:	Aspartic acid
Cys	:	Cysteine
Gln	:	Glutamine
Glu	:	Glutamic acid
Gly	:	Glycine
His	:	Histidine
Ile	:	Isoleucine
Leu	:	Leucine
Lys	:	Lysine
Met	:	Methionine
Phe	:	Phenylalanine
Pro	:	Proline
Ser	:	Serine
Thr	:	Threonine
Trp	:	Tryptophan
Tyr	:	Tyrosine
Val	:	Valine
SD	:	Standard Deviation
H_2O_2	:	Hydrogen Peroxide
CM-H_2DCFDA	:	5-(6)-Chloromethyl-2′,7′-dichlorodihydrofluorescein diacetate, acetyl ester
PBS	:	phosphate buffer saline
RT	:	room temperature
PI	:	propidium iodide
PB	:	phosphate buffer
PS	:	phosphatidylserine

FITC	:	Fluorescein Isothiocyanate
MMP	:	mitochondrial membrane potential
CMXRos	:	Chloromethyl-X-rosamine
PFA	:	paraformaldehyde
GBM cell lines	:	Glioblastoma Multiforme cell lines
PI3K	:	Phosphoinositide 3-kinase
Akt	:	RAC-alpha serine/threonine-protein kinase
mTOR	:	mechanistic target of rapamycin
FeSODA	:	Iron-superoxide dismutase A
NAD	:	Nicotinamide Adenine Dinucleotide

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