

Studies on Anti-Leishmanial Compound Discovery



Thesis submitted in partial fulfilment for the

Award of Degree

Doctor of Philosophy

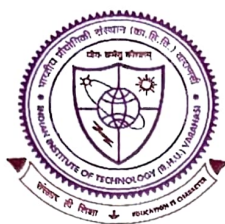
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I, **Naveena Menpadi**, certify that the work embodied in this thesis is my own bona fide work and was carried out by me under the supervision of **Prof. Vikash Kumar Dubey** and **Dr. Pranjal Chandra** from **July 2019 to July 2025**, at the School 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.....*

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Naveena Menpadi
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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	: <i>Leishmania donovani</i> 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
R _g	: 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 ₂ O ₂	: Hydrogen Peroxide
CM-H ₂ DCFDA	: 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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