

CONTENTS

Subject	Page No.
Abstract	i-v
Declaration	vi
Certificate	vii
Acknowledgement	viii-ix
Contents	x-xiv
List of Tables	xv-xvi
List of Figures	xvii-xx
List of Abbreviations	xxi-xxii

Chapter 1	Introduction	Page no.
1.1	Leishmaniasis- An overview	1
1.2	Etiology	1-2
1.3	Epidemiology	2-4
1.4	Leishmaniasis treatment	5
1.4.1	Chemotherapy	6-7
1.4.2	Immunotherapy	7-8
1.4.3	Nanoparticles therapy	8-10
1.5	Development of vaccines against Leishmaniasis	10
1.5.1	First Generation Vaccines of Leishmaniasis	11
1.5.2	Second generation vaccines of Leishmaniasis	12
1.5.3	Third generation vaccines of Leishmaniasis	13
1.6	Drug resistance in Leishmaniasis	14-16
1.7	Drug discovery approaches against Leishmaniasis	17
1.8	Multitarget approach	17-18
1.9	Drug repurposing approach	18-19
1.10	Subtractive genomics approach	20
1.11	Scope of the work	21-22
Bibliography		23-32

Chapter 2	Methodology	Page no.
2.1	Selection of protein targets	33
2.2.	Protein structure preparation	34
2.2.1	Details of Homology Modeling	33-35
2.2.2	Binding site prediction of protein structure	36
2.3	Screening of Ligands	36
2.3.1	Collection of ligands	37-38
2.3.2	Ligands filtration	38-40
2.4	Molecular Docking	40
2.5	Method of Subtractive genomics	41
2.5.1	Collection of proteomes	42
2.5.2	Data Filtration	42-43
2.5.3	Druggability analysis and identification of novel drug targets	44
2.6	Insights from Molecular Dynamics Simulations	44-45
2.6.1	Understanding force fields in molecular dynamics simulations	45-48
2.6.2	Ensemble	48
2.6.3	Understanding Periodic Boundary Conditions	49
2.6.4	Particle mesh Ewald Summation	50
2.6.5	Structure preparation	50-51
2.6.6	System preparation	51
2.6.7	Binding energy calculations	51-52
Bibliography		53-60
Chapter 3	To study multiple proteins of <i>Leishmania donovani</i> and finding out potential compounds for its inhibition	Page no.
3.1	Abstract	61

3.2.	Introduction	61-65
3.3.	Methodology	65
3.3.1	Protein and ligand structure retrieval	65-66
3.3.2	Screening of ligands	66-67
3.3.3	Molecular docking studies	67
3.3.4	Molecular Dynamic Simulation	67-68
3.3.5	Binding energy calculations	68
3.4	Results	68
3.4.1	Details of APRT and DHODH protein sequences and their mechanics	68-69
3.4.2	Analysis of screened ligands	70-73
3.4.3	Binding affinity prediction of drug molecules	73-77
3.4.4	MD simulation: trajectory analyses of APRT and DHODH with ligands	78-84
3.4.5	Non-bonded Contacts Analysis	84-87
3.4.6	MMPBSA analysis: energetics of APRT and DHODH with compounds	88-89
3.4.7	Per-residue energy contributions to binding	89-91
3.5	Discussion	92-94
Bibliography		95-100

Chapter 4	Repurposing of potential anti-parasitic inhibitors against specific <i>Leishmania</i> protein targets	Page no.
4.1	Abstract	101
4.2	Introduction	101-105
4.3	Methodology	105
4.3.1	Protein selection and ligand collection	105-106
4.3.2	Screening of ligands	106
4.3.3	Molecular docking studies	107
4.3.4	Molecular Dynamics Simulations	107
4.3.5	Binding energy calculations	107
4.4	Results	107-111

4.4.1	Details of Pyridoxal kinase and Sterol 14-alpha demethylase protein sequences	112
4.4.2	Ligands screening and analysis	113
4.4.3	Molecular docking analysis	113-115
4.4.4	MD simulations: trajectory analyses	116
4.4.5	Structure change analysis	116-117
4.4.6	Stability analysis	118
4.4.7	Residue fluctuation analysis	118
4.4.8	Radius of gyration analysis	119
4.4.9	Hydrogen bond interaction analysis	120
4.4.10	Non-bonded analysis	120-123
4.5	MMPBSA and binding free energy analysis	124-125
4.6	Discussion	125-127
Bibliography		128-133

Chapter 5	Comparative genome analysis of different strains of <i>Leishmania</i> species using available sequences	Page no.
5.1	Abstract	134
5.2	Introduction	134-137
5.3	Materials and Methods	137
5.3.1	Data collection and screening of proteins	138
5.3.2	Identification of orthologous groups and non-homologous sequences	138
5.3.3	Druggability analysis and identification of novel drug targets	139
5.3.4	Protein active site prediction and molecular docking studies	139
5.3.5	Molecular Dynamic Simulations	140
5.4	Results	140
5.4.1	Data collection of proteomes and protein sequence exclusion	140-141
5.4.2	Analysis of orthologous groups and non-homologous protein	141-142

5.4.3	Druggability analysis and drug target identification	142-145
5.4.4	Analysis of protein target	145-147
5.4.5	Active site prediction of proteins and molecular docking analysis	147-151
5.4.6	MD simulation analysis	152-156
5.4.7	Interaction analysis	156-159
5.4.8	MMPBSA and binding free energy analysis	159-160
5.5	Discussion	160-163
Bibliography		164-167

Chapter 6	Summary and Future prospects	168-171
------------------	------------------------------	---------