LIST OF FIGURES

Fig. No.	PARTICULARS	PAGI NO.
	Literature review	
2.1	Structure of quercetin.	15
2.2	Structure of taxifolin.	17
	Results and discussion	
4.1	Ligand docked Bcl-2: Left; quercetin (upper-surface presentation of Bcl-2-quercetin complex, lower-2D plot of interaction of quercetin with Bcl-2), Right; taxifoin (upper- surface presentation of Bcl-2-taxifoin complex, lower-2D plot of interaction of taxifolin with Bcl-2).	38
4.2	(A) Plot of root mean square deviation (RMSD) of backbone of Bcl-2 bound to quercetin (black) and taxifolin complex (grey),(B) Plot of root mean square deviation (RMSD) of quercetin (black) and taxifolin (grey) in hydrophobic groove of Bcl-2.	39-40
4.3	Profile of (A) Coulombic interaction energy, (B) van der Waals (vdW) interaction energy between Bcl-2-quercetin (black) and Bcl-2-taxifolin (grey).	40
4.4	2D presentation of interaction of quercetin with Bcl-2 residues at different time of MD simulation.	41
4.5	2D presentation of interaction of taxifolin with Bcl-2 residues at different time of MD simulation.	42
4.6	Comparison of surface structure of Bcl-2 crystal structure and ligand bound Bcl-2 after 10 ns MD simulation.	43
4.7	Ligand docked Bcl-2-Bax complex (A) quercetin (upper-cartoon presentation of Bcl-2-Bax-quercetin complex, lower-2D plot of interaction of quercetin with Bcl-2-Bax complex), (B) taxifoin (upper-cartoon presentation of Bcl-2-Bax-taxifoin complex, lower-2D plot of interaction of taxifolin with Bcl-2-Bax complex), (C) obatoclax (upper-cartoon presentation of Bcl-2-Bax- obatoclax complex, lower-2D plot of interaction of obatoclax with Bcl-2-Bax complex).	44-45
4.8	(A) RMSD profile of Bcl-2-Bax backbone, (B) conformations of	46

Bcl-2-Bax complex during 12 ns MD simulation. 4.9 (A) RMSD profile of taxifolin bound Bcl-2-Bax complex 47 backbone, (B) conformations of taxifolin bound Bcl-2-Bax complex during 12 ns MD simulation showed dissociation of complex. 4.10 48 (A) RMSD profile of quercetin bound Bcl-2-Bax complex backbone, (B) conformations of guercetin bound Bcl-2-Bax complex during 12 ns MD simulation showed dissociation of complex. 4.11 49 (A) RMSD profile of obatoclax bound Bcl-2-Bax complex backbone, (B) conformations of obatoclax bound Bcl-2-Bax complex during 12 ns MD simulation showed insignificant dissociation effect. 4.12 **50** RMSF of Bcl-2 residues backbone (upper) and Bax residues backbone (lower) during MD simulation. 4.13 51 RMSF of Bcl-2 residues side chain (upper) and Bax residues side chain (lower) during MD simulation. The Hsp90-ATP-binding site and taxifolin interaction. 52 4.14 4.15 (A) Plot of root mean square deviation (RMSD) of backbone of 53 Hsp90 unbound (black) and Hsp90–taxifolin complex (red), (B) Plot of root mean square deviation (RMSD) of taxifolin. The trajectories were captured every 0.5 ps until the simulation time reached 10,000 ps. Number of H-bonds formed between taxifolin and Hsp90 during 54 4.16 10,000 ps MD simulation. 2D plots of interaction between taxifolin and Hsp90 at different 4.17 55 time interval of MD simulation. 4.18 (A) Radius of gyration of Hsp90 unbound (black) and Hsp90-**56** taxifolin complex (red), (B) RMSF of Hsp90 backbone (black) and Hsp90-taxifolin backbone (red). (A) ATP bound "closed" or "lid-down" conformation of Hsp90 58 4.19 N-terminal domain, (B) ADP bound "open" or "lid-up" conformation of Hsp90 N-terminal domain, (C) Geldanamycin bound "open" or "lid-up" conformation of Hsp90 N-terminal domain, (D) Taxifolin bound "open" or "lid-up" conformation of

Hsp90 N-terminal domain after 10,000 ps MD simulation.

4.20

(A) Plot of root mean square deviation (RMSD) of backbone of

60

- Hsp90–cdc37 unbound (black) and Hsp90–cdc37–taxifolin complex (red). (B) Plot of root mean square deviation (RMSD) of taxifolin.
- 4.21 (A) Potential energy profile of Hsp90–cdc37 unbound (black) and Hsp90–cdc37–taxifolin complex (red) during 10,000 ps MD simulation. (B) Number of H-bonds formed between taxifolin and Hsp90–cdc37 interface residues during 10,000 ps MD simulation.
- 4.22 2D plots of interaction between taxifolin and Hsp90–cdc37 complex at different time interval of MD simulation.
- 4.23 (A) RMSF of Hsp90 residues backbone (black) in Hsp90–cdc37 complex (taxifolin unbound) and Hsp90 residues backbone (red) in Hsp90–cdc37 complex (taxifolin bound), (B) RMSF of Cdc37 residues backbone (black) in Hsp90–cdc37 complex (taxifolin unbound) and Cdc37 residues backbone (red) in Hsp90–cdc37 complex (taxifolin bound).
- 4.24 (A) RMSF of Hsp90 residue side chains (black) in Hsp90–cdc37 complex (taxifolin unbound) and Hsp90 residue side chains (red) in Hsp90–cdc37 complex (taxifolin bound), (B) RMSF of Cdc37 residue side chains (black) in Hsp90–cdc37 complex (taxifolin unbound) and Cdc37 residue side chains (red) in Hsp90–cdc37 complex (taxifolin bound).
- 4.25 (A) Interaction between Arg167 of Cdc37 and Glu 47 of Hsp90 in taxifolin unbound form, (B) Interaction between Arg166 and, Arg167 of Cdc37 and Gln133 of Hsp90 in taxifolin unbound form, (C) Disruption of interaction between Arg167 of Cdc37 and Glu 47 of Hsp90 in taxifolin bound form, (D) Disruption of interaction between Arg166 and, Arg167 of Cdc37 and Gln133 of Hsp90 in taxifolin bound form.
- 4.26 (A) Interaction between Ala 204, and Leu 205 of Cdc37 and Lys 116, and Glu 120 of Hsp90 in taxifolin unbound form, (B) Interaction between Ala 204 and, Leu 205 of Cdc37 and Lys 116, and Glu 120of Hsp90 in taxifolin bound form, (C) Interaction between Asp 170 of Cdc37 and Gln 133 of Hsp90 in taxifolin unbound form, (D) Disrupted interaction between Asp 170 of Cdc37 and Gln 133 of Hsp90 in taxifolin bound form.
- 4.27 (A) Quercetin bound to hydrophobic groove of MDM2 and 2D 68

62

	hydrophobic groove of MDM2 and 2D presentation of interaction with residues.	
4.28	(A) Plot of root mean square deviation (RMSD) of backbone of MDM2 complexed with quercetin (black) and with taxifolin (grey), (B) Plot of root mean square deviation (RMSD) of quercetin (black) and taxifolin (grey) in hydrophobic groove of MDM2.	69
4.29	Comparison of last pose of 65 ns MD simulation of MDM2 in ligands bound form with apo and chromeno-triazolopyrimidine complexed MDM2.	70
4.30	Comparison of interaction of last pose of 65 ns MD simulation of MDM2 with ligands and benzodiazepine, and chromenotriazolopyrimidine complexed MDM2.	71
4.31	(A) Plot of root mean square deviation (RMSD) of backbone of MDM2-p53 complexed with taxifolin (grey), MDM2-p53 complexed with quercetin (black) and without ligand (red), (B) Plot of root mean square deviation (RMSD) of taxifolin (grey) and quercetin (black).	74
4.32	(A) Number of H-bonds formed between taxifolin and MDM2-p53 interface residues, (B) Number of H-bonds formed between quercetin and MDM2-p53 interface residues during 12 000 ps MD simulation.	75
4.33	RMSF of MDM2-p53 residues backbone in taxifolin bound (black), quercetin bound (grey) and ligand unbound form (light grey).	75-76
4.34	Snap shots at different time interval of MDM2-p53 complexed with taxifolin for 15 000 ps MD simulation showing dissociation of complex.	76
4.35	Snap shots at different time interval of MDM2-p53 complexed with quercetin for 15 000 ps MD simulation showing dissociation of complex.	77
4.36	2D plots of interaction between taxifolin and MDM2-p53 at different time interval of 15 000 ps MD simulation.	78
4.37	2D plots of interaction between quercetin and MDM2-p53 at different time interval of 15 000 ps MD simulation.	79

presentation of interaction with residues, (B) Taxifolin bound to

4.38	(A) Bindinding of taxifolin at ATP-binding site on VEGFR-2 kinase: surface view and ribbon structure, (B) Stereo view of H-	80
	bond pattern of taxifolin with ATP-binding pocket residues.	
4.39	Plot of root mean square deviation (RMSD) of backbone of VEGFR-2 unbound (red) and VEGFR-2-taxifolin complex	81
	(black).	
4.40	Number of H-bonds formed during 3800 ps MD simulation.	82
4.41	Root mean square fluctuation (RMSF) of VEGFR-2 unbound (red) and VEGFR-2 kinase-taxifolin (black) atoms during 3800 ps MD simulation.	83
4.42	Root mean square fluctuation (RMSF) of ATP-binding pocket residues (1-15: Leu 868, Glu 883, Lys 885, Glu 915, Phe 916, Cys 917, Lys 918, Phe 919, Gly 920, Asn 921, Leu 926, Arg 927, Ser 1035, Asp 1044 and Lys 1053) of VEGFR-2 unbound (red) and VEGFR-2 kinase-taxifolin (black) during MD simulation.	83
4.43	Snapshot of system (VEGFR-2, taxifolin, water and counterions) at 3800 ps and conformational changes occurs in VEGFR-2 kinase during MD simulation (purple-0 ps, blue- 3800 ps, green-position of activation loop at 0 ps and yellow- position of activation loop at 3800 ps).	85
4.44	Effect of quercetin on viability of HeLa cells. Data are represented as mean±SD of three determinations each performed in triplicate.	86
4.45	Effect of taxifolin on viability of HeLa cells. Data are represented as mean±SD of three determinations each performed in triplicate.	86
4.46	(A) Quercetin-induced DNA fragmentation in HeLa cells, (B) taxifolin-induced DNA fragmentation in HeLa cells	87
4.47	Effect of quercetin on markers of intrinsic apoptosis in HeLa cells by RT-PCR analyses	88
4.48	Effect of taxifolin on markers of intrinsic apoptosis in HeLa cells by RT-PCR analyses.	88

5.1 Schematic representation of in silico and in vitro studies of quercetin and taxifolin on different molecular target and HeLa cells.