Electronic Supplementary Material (ESI) for RSC Advances.

Exploring Cyclin-Dependent Kinase Inhibitors: A Comprehensive Study in Search of CDK-6 Inhibitors using Pharmacophore Modelling and Dynamic Approach

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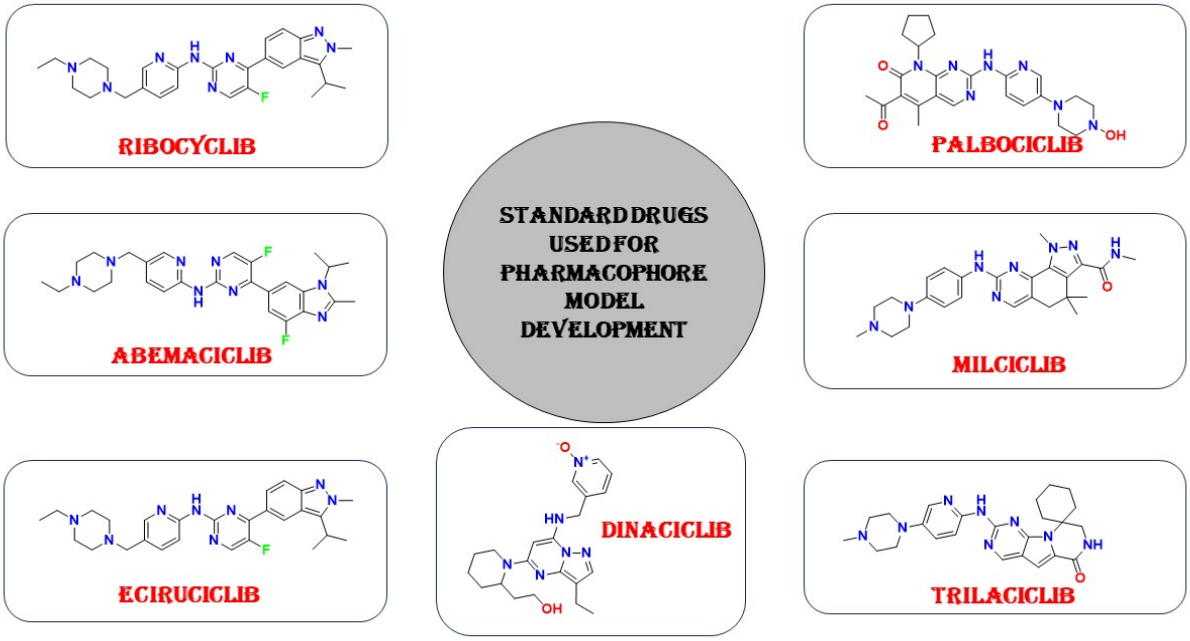

Fig. S1 Approved CDK inhibitor drugs used for Pharmacophore model development.

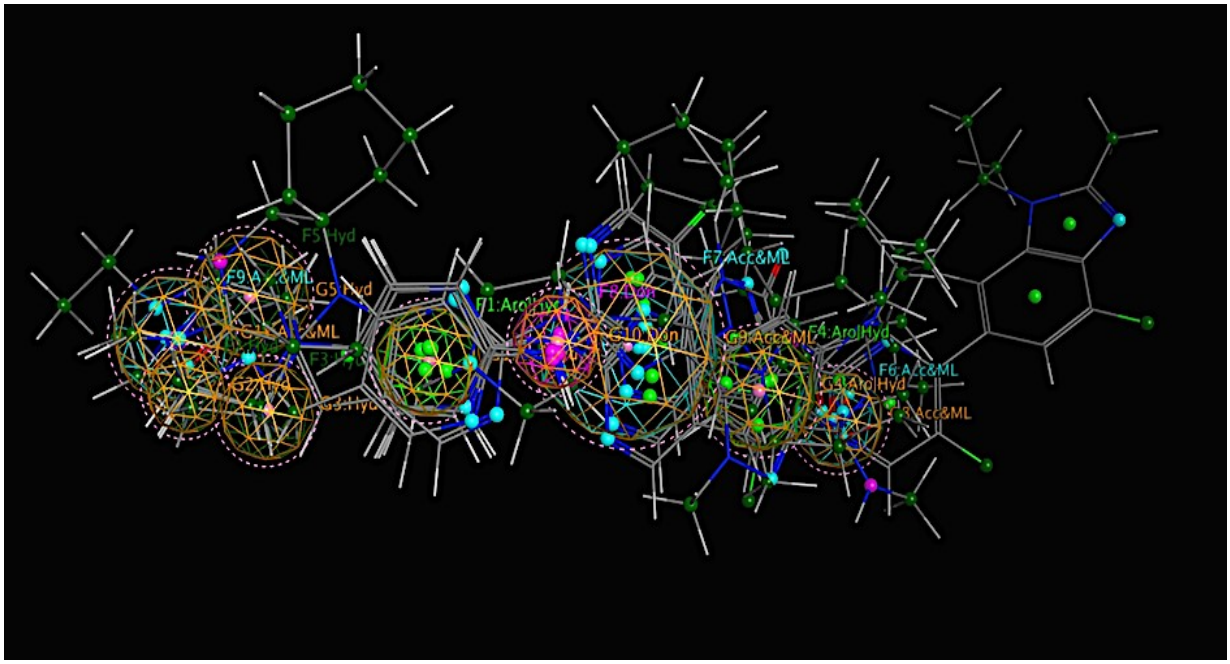

Fig. S2 Pharmacophoric features and Flexible alignment of standard drugs

a)

b)

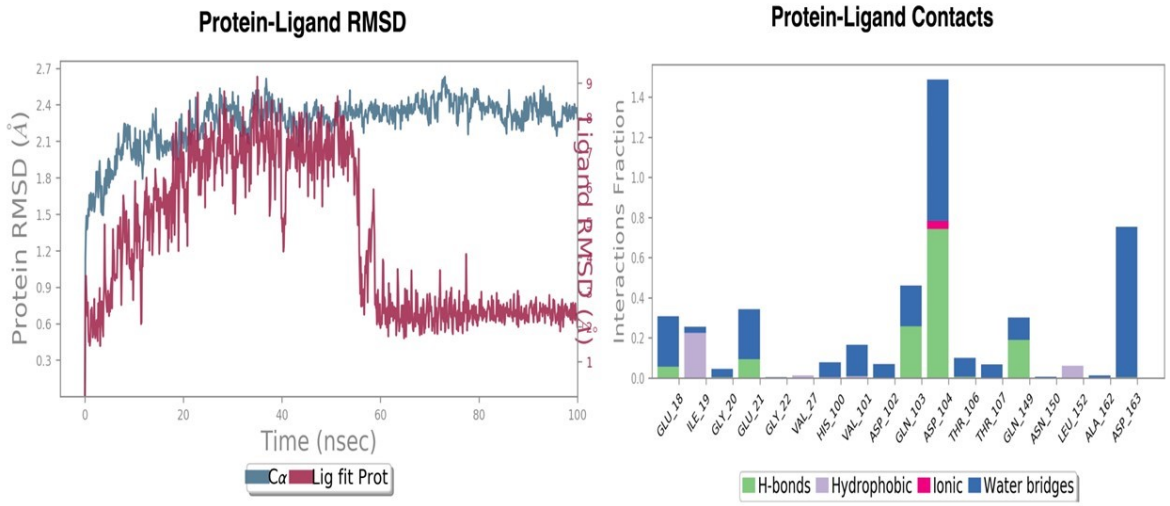

Fig. S3 a) RMSD plot of ligand fit protein of compound 18.

b) H-bond plot of compound 18.

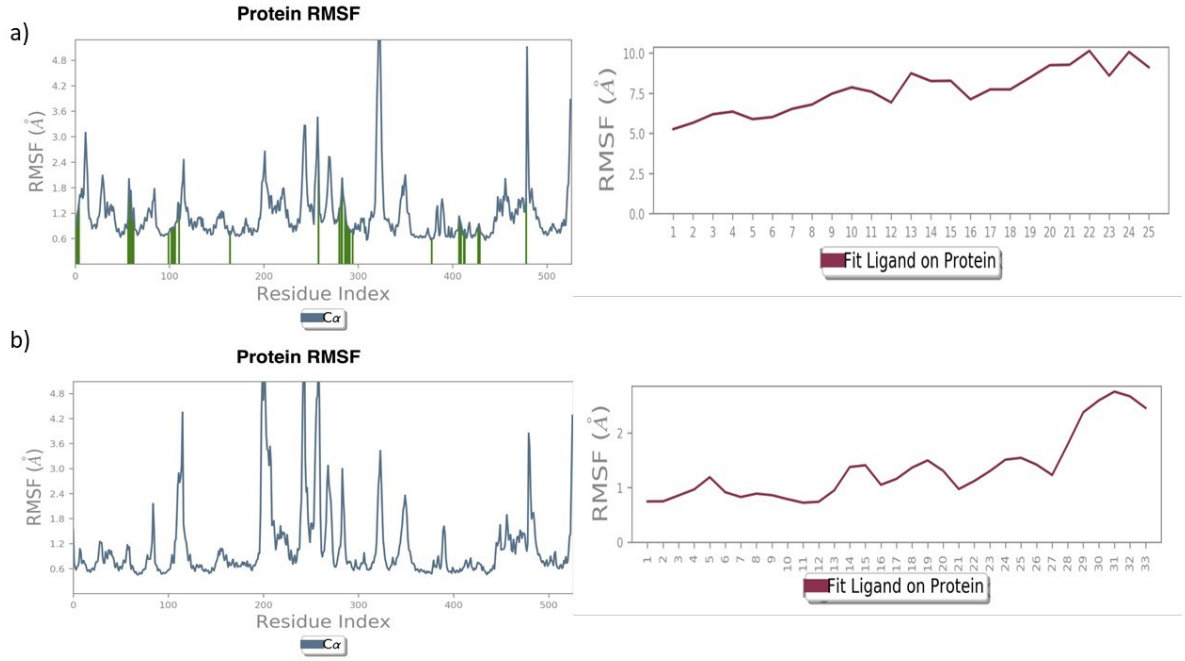

Fig. S4 a) Protein RMSF Reference and Ligand RMSF of Compound-6

b) Protein RMSF Reference and Ligand RMSF of Standard.

Table S1 Physico Chemical parameters of the designed compounds

Ligand ID	log P	TPSA	MW	HBA	HBD	No of rotatable bonds	No of violations
B1	1.54	90.04	314.74	4	2	2	0
B2	1.59	99.27	344.76	5	2	3	0
B3	2.22	90.04	349.18	4	2	2	0
B4	1.50	135.86	359.73	6	2	3	0
B5	1.48	110.27	330.74	5	3	2	0

B6	0.88	119.50	360.76	6	3	3	0
B7	1.08	119.50	360.76	6	3	3	0
B8	0.78	130.50	346.73	6	4	2	0
B9	0.98	130.50	346.73	6	4	2	0
B10	0.51	150.72	362.73	7	5	2	0
B11	1.55	99.27	344.76	5	2	3	0
B12	1.57	99.27	344.76	5	2	3	0
B13	1.36	108.51	374.79	6	2	4	0
B14	1.56	108.51	374.79	6	2	4	0
B15	1.37	117.74	404.81	7	2	5	0
B16	1.17	110.27	404.81	7	2	5	0
B17	1.03	130.50	330.74	5	3	2	0
B18	0.51	150.72	346.73	6	4	2	0
B19	0.28	110.27	362.73	7	5	2	0
B20	1.06	90.04	330.74	5	3	2	0
B21	1.99	90.04	328.76	4	2	2	0
B22	2.32	90.04	393.63	4	2	2	0
B23	2.17	90.04	349.18	4	2	2	0
B24	2.19	90.04	349.18	4	2	2	0
B25	2.80	90.04	383.63	4	2	2	0
B26	3.43	90.04	418.07	4	2	2	0
B27	0.25	102.93	315.72	5	2	2	0
B28	0.37	102.93	315.72	5	2	2	0
B29	0.80	103.18	304.70	5	2	2	0
B30	2.35	90.04	393.63	4	2	2	0

Table S2 Bioactivity score of designed compounds

Ligand ID	GPCR ligand	Ion channel module	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
B1	-0.12	-0.42	0.01	-1.07	-0.62	-0.32
B2	-0.14	-0.46	-0.02	-0.97	-0.59	-0.35
B3	-0.10	-0.41	0.00	-1.02	-0.61	-0.34
B4	-0.25	-0.43	-0.12	-1.02	-0.65	-0.40
B5	-0.10	-0.38	0.01	-0.90	-0.58	-0.27
B6	-0.11	-0.42	0.02	-0.88	-0.59	-0.28
B7	-0.13	-0.39	-0.01	-0.94	-0.61	-0.30
B8	-0.07	-0.32	0.03	-0.90	-0.56	-0.24
B9	-0.08	-0.36	0.04	-0.78	-0.55	-0.24
B10	-0.09	-0.31	0.04	-0.87	-0.53	-0.20
B11	-0.15	-0.45	-0.06	-0.97	-0.62	-0.35
B12	-0.14	-0.48	-0.04	-0.96	-0.60	-0.35
B13	-0.16	-0.44	-0.08	-0.97	-0.60	-0.35
B14	-0.13	-0.43	-0.02	-0.89	-0.56	-0.31
B15	-0.17	-0.42	-0.07	-0.94	-0.58	-0.33
B16	-0.15	-0.42	-0.05	-0.84	-0.57	-0.31
B17	-0.06	-0.37	0.05	-0.85	-0.57	-0.26
B18	-0.05	-0.35	0.07	-0.79	-0.53	-0.23
B19	-0.07	-0.34	0.07	-0.84	-0.50	-0.20
B20	-0.05	-0.35	0.07	-0.85	-0.56	-0.25
B21	-0.15	-0.48	-0.03	-1.04	-0.63	-0.37
B22	-0.22	-0.49	-0.06	-1.15	-0.72	-0.40
B23	-0.12	-0.44	-0.11	-1.00	-0.68	-0.39
B24	-0.09	-0.40	-0.01	-1.03	-0.61	-0.34
B25	-0.09	-0.39	-0.14	-0.95	-0.63	-0.37
B26	-0.11	-0.45	-0.21	-0.87	-0.67	-0.35
B27	-0.09	-0.37	0.10	-1.09	-0.60	-0.27
B28	-0.05	-0.30	0.13	-1.16	-0.58	-0.28
B29	-0.31	-0.67	-0.33	-1.33	-1.01	-0.49

B30	-0.21	-0.48	-0.03	-1.12	-0.70	-0.39

Table S3 ADMET Studies

Ligand ID	LIVER TOXICITY		METABOLISM Cyp inhibitors						BBB	P-gp inhibitor	P-gp substrate	Herg Blocker	MMP	AMES
	DILI	CYTOTOXIC	HLM	1A2	3A4	2D6	2E9	2C19						
B1	Yes	No	Yes	No	No	No	No	No	Yes	No	No	Yes	No	Yes
B2	Yes	No	Yes	No	No	No	No	No	Yes	Yes	Yes	No	No	Yes
B3	Yes	No	Yes	No	No	No	No	No	Yes	No	No	Yes	No	No
B4	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	Yes
B5	Yes	No	Yes	No	No	No	No	No	Yes	No	No	No	No	Yes
B6	Yes	No	Yes	No	No	No	No	No	Yes	Yes	No	No	No	No
B7	Yes	No	Yes	No	No	No	No	No	No	No	Yes	No	No	Yes
B8	Yes	No	Yes	No	No	No	No	No	Yes	No	No	No	No	Yes
B9	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	Yes
B10	Yes	No	Yes	No	No	No	No	No	Yes	No	No	No	No	Yes
B11	Yes	No	Yes	No	No	No	No	No	Yes	Yes	Yes	Yes	No	Yes
B12	Yes	No	No	No	No	No	No	No	Yes	Yes	Yes	Yes	No	Yes
B13	Yes	No	Yes	No	No	No	No	No	No	Yes	Yes	No	No	Yes
B14	Yes	No	Yes	No	No	No	No	No	No	No	Yes	Yes	No	Yes
B15	Yes	No	Yes	No	No	No	No	No	No	Yes	Yes	No	No	Yes
B16	Yes	No	Yes	No	No	No	No	No	Yes	No	Yes	Yes	No	Yes
B17	Yes	No	Yes	No	No	No	No	No	Yes	No	No	Yes	No	Yes
B18	Yes	No	Yes	No	No	No	No	No	Yes	No	No	No	No	Yes
B19	Yes	No	Yes	No	No	No	No	No	Yes	No	No	No	No	Yes
B20	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No
B21	Yes	No	Yes	No	No	No	No	No	Yes	Yes	No	No	No	Yes
B22	Yes	No	Yes	No	No	No	No	No	Yes	Yes	No	Yes	No	Yes
B23	Yes	No	Yes	No	No	No	No	No	Yes	Yes	No	Yes	No	Yes
B24	Yes	No	Yes	No	No	No	No	No	Yes	Yes	No	Yes	No	No
B25	Yes	No	Yes	No	No	No	No	No	Yes	Yes	No	No	No	Yes
B26	Yes	No	Yes	No	No	No	No	No	Yes	Yes	No	No	No	No
B27	Yes	No	Yes	No	No	No	No	No	Yes	No	No	Yes	No	Yes
B28	Yes	No	Yes	No	No	No	No	No	Yes	No	No	Yes	No	Yes
B29	Yes	No	Yes	No	No	No	No	No	Yes	No	No	Yes	No	Yes
B30	Yes	No	Yes	No	No	No	No	No	Yes	Yes	No	No	No	Yes