International Journal of Research in Engineering and Science (IJRES)
ISSN (Online): 2320-9364, ISSN (Print): 2320-9356
www.ijres.org Volume 11 Issue 5 ǁ May 2023 ǁ PP. 775-779

Molecular Docking of Small Amide Molecules with CDK-2 Enzyme for Anticancer Activity

Arun Kumar*[1], Pawan Kumar[2],Markandey Mishra[1], Jaiprakash Kasaudhan[1], Gayatri Devi[1], Maya Chaudhary[1], Mohd Arif[1] and Ahmad Raza[1]

Affilation:[1]Maharani Lal Kunwari P.G. College, Balrampur, UP-271201.[2]Acharya Narendra Dev College, Kalkaji, New Delhi.

Email: ar83_kumar@rediffmail.com

Corresponding address: Dr. Arun Kumar, Assistant Professor, Department of Chemistry, M.L.K. P.G. College, Balrampur, UP-271201.

Abstract

In this work we have designed the compounds inspired from the literature and performed the molecular docking study. The molecular docking of designed compounds were performed with the CDK-2 enzyme (PDB Id: 2FVD) for the enzyme inhibition. The CDK-2 enzyme involves in the cancer cell cycle to cell growth. Here the compounds were showed the various hydrogen bonding interactions and good docking energy for the enzyme inhibition.

Date of Submission: 14-05-2023 Date of acceptance: 26-05-2023

I. Introduction

Cancer is a malignant tumour which is lethal disease and affects the highly number of human population in the world[1]. Nowadays the number of cancer patients increases day by day which is a globally health problem. As from the earlier time various types of natural products[2], synthetic drugs[3] and other treatments were used to inhibit the tumour growth. The mechanism of action of these drugs and natural products were different to stop the cancer cell cycle, inhibit the enzyme responsible for cancer cell growth and DNA intercalation etc. But to improvement in drug efficacy, reduced side effects and for easily availability a number of research groups actively working on anticancer agents[4]. Generally in the drug design and development procedure some steps involve as computational chemistry[5] (molecular design and docking etc), synthetic chemistry[6]and biological studies[7].

II. Results and Discussion

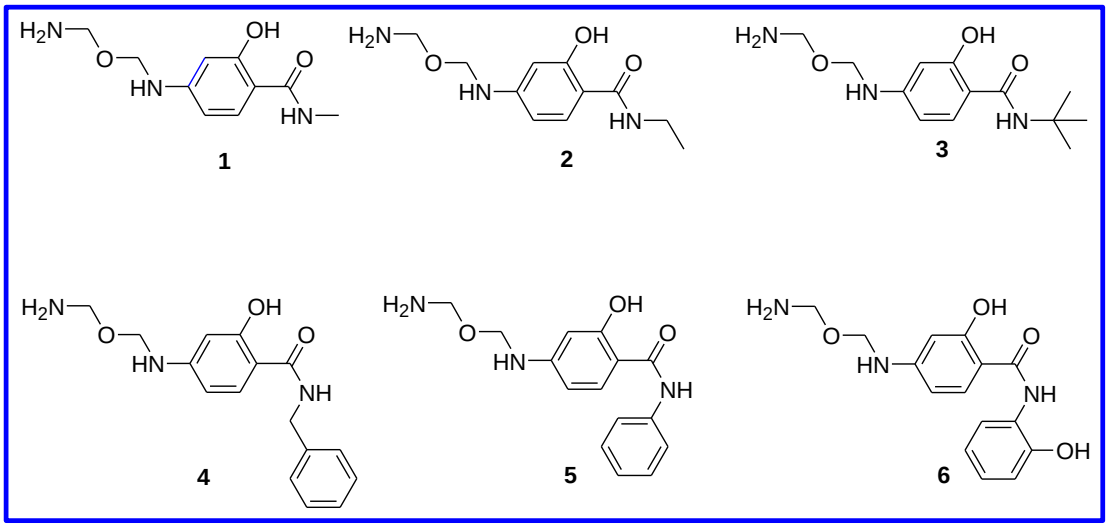


Figure 1: structures of designed compounds.

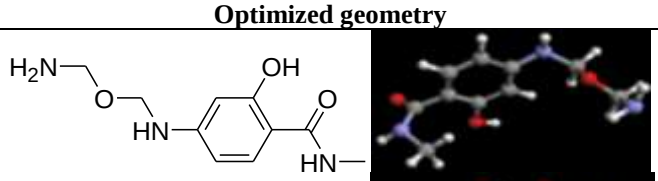
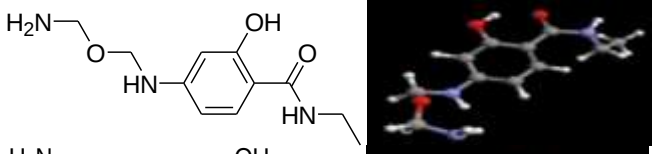
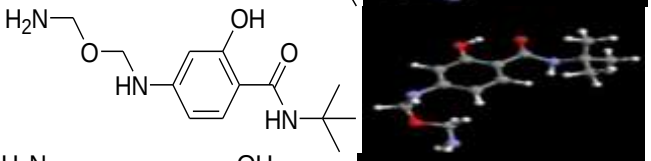
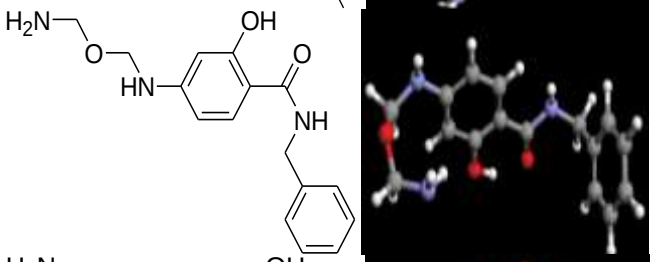
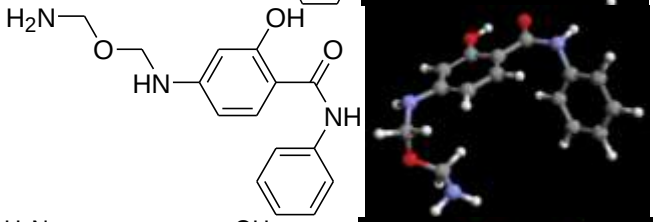
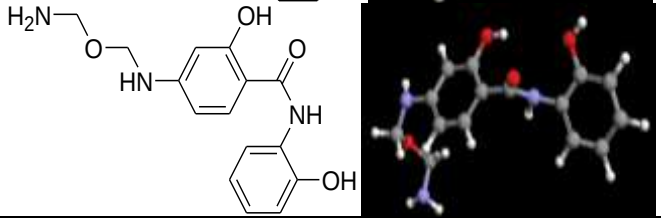
In this project we have worked on the computational chemistry branch to the inhibition of enzyme activity responsible for the tumour growth. From the literature[8-10] survey we have designed the molecules and used for the molecular docking to inhibit the enzyme CDK-2 function which regulates the cancer cell cycle. The physical parameters of the compounds (**1 to 6**) were showing good lipophilicity (Table 1).

Table 1: Physical parameters of compound **1** to **6** according to Lipinski rule of 5.

Parameters	Comp. 1	Comp. 2	Comp. 3	Comp. 4	Comp. 5	Comp. 6
miLogP	0.82	1.20	2.01	2.22	2.52	2.25
TPSA	96.61	96.61	96.61	96.61	96.61	116.84
natoms	16	17	19	22	21	22
MW	225.25	239.28	267.33	301.35	287.32	303.32
nON	6	6	6	6	6	7
nOHNH	5	5	5	5	5	6
volume	206.29	223.09	255.91	277.94	261.13	269.15

The energy optimization (figure 2) of compounds (**1-6)** was done by Argus Lab software for the docking procedure.

Figure 2: Energy optimization figures of compounds **1-6**.

S. NO.	Compound	Optimized geometry
1	**1**	
2	**2**	
3	**3**	
4	**4**	
5	**5**	
6	**6**	

Molecular docking of compounds **1** to **6** was performed with CDK-2 enzyme (PDB Id: 2FVD) by Argus Lab software. After the completion of docking study we have found the various types of interactions (figure 3-8 and Table 2-6) between the compound **1-6** and enzyme (CDK-2) binding site. The compound 1, 2, 3, 4, 5 and 6 were

showing different hydrogen bonding interactions and docking energies as – 8.24 kcal/mole, -8.60 kcal/mole, -8.99 kcal/mole, -10.82 kcal/mole, -10.50 kcal/mole and -9.72 kcal/mole respectively.

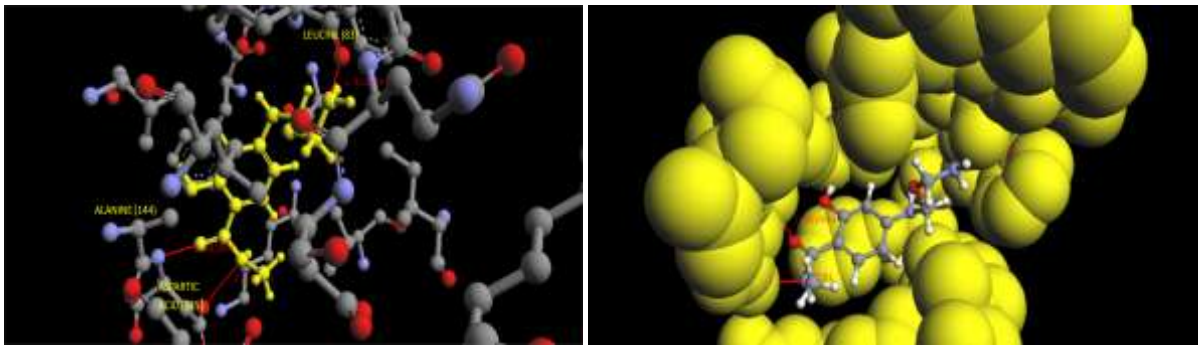


Figure 3: Molecular docking structure of compound **1** with CDK-2 enzyme (PDB Id: 2FVD).

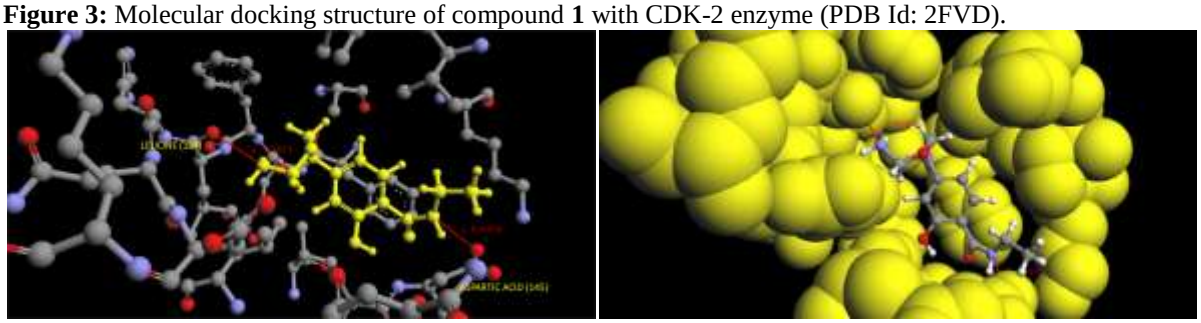


Figure 4: Molecular docking structure of compound **2** with CDK-2 enzyme (PDB Id: 2FVD).

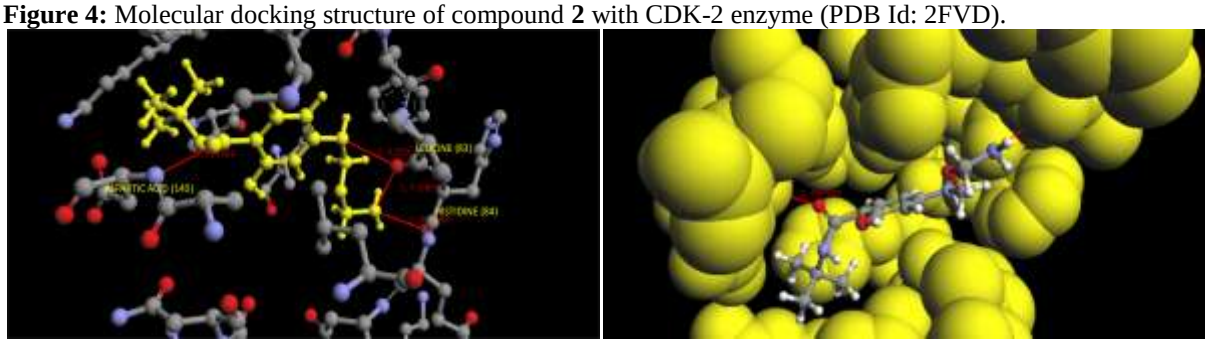


Figure 5: Molecular docking structure of compound **3** with CDK-2 enzyme (PDB Id: 2FVD).

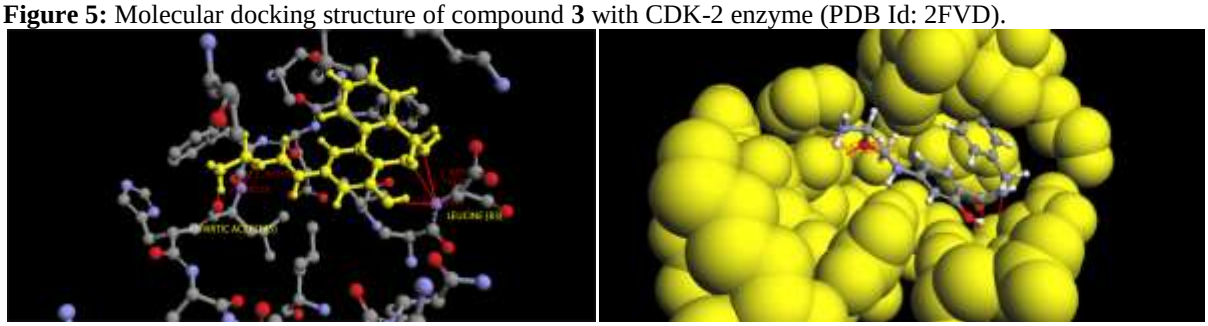


Figure 6: Molecular docking structure of compound **4** with CDK-2 enzyme (PDB Id: 2FVD).

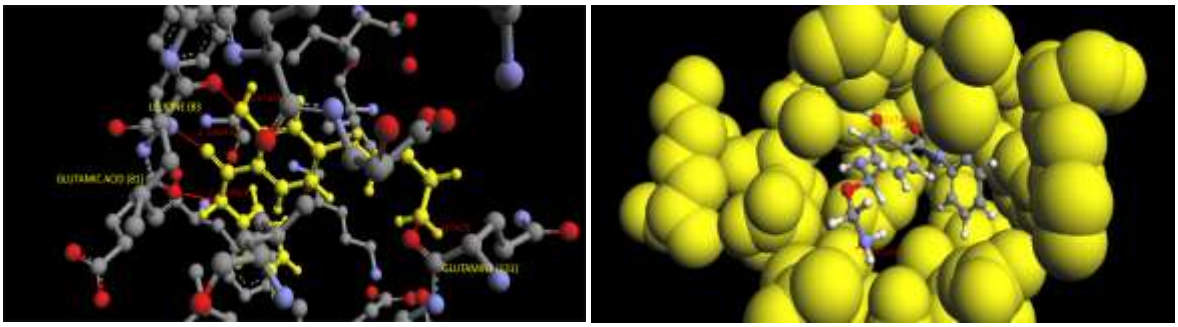


Figure 7: Molecular docking structure of compound **5** with CDK-2 enzyme (PDB Id: 2FVD).

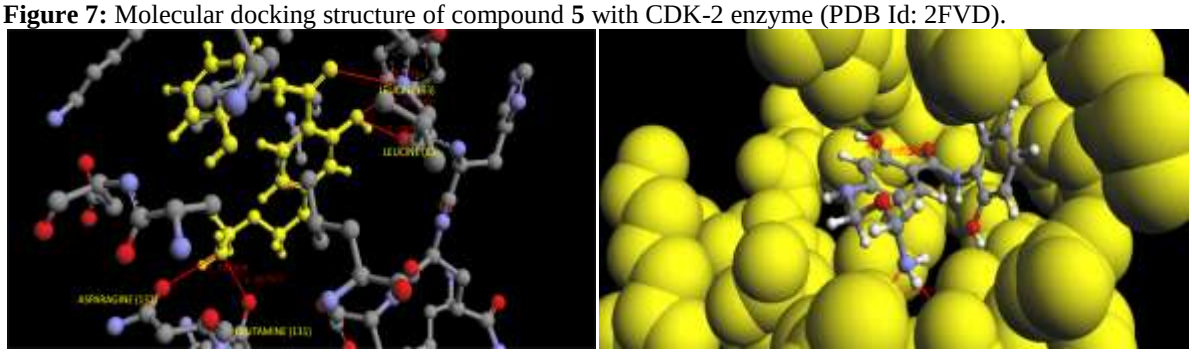


Figure 8: Molecular docking structure of compound **6** with CDK-2 enzyme (PDB Id: 2FVD).

Table 2: Molecular docking results of compound **1** with CDK-2 enzyme.

S. NO.	**DOCKING STUDY**		
1.	**H-bond interactions**		
	H-bond distance (in angstrom)	**Molecule part involved**	**Active site of Enzyme**
a.	2.50	Amidic -C=O	β-strand of Alanine (144)
b.	2.93	Amidic -NH	Aspartic acid coil (145)
c.	1.92	Free $-NH_2$ of side chain	β-strand of Leucine (83)
2.	**Best Ligand Pose Energy (Docking energy)**		
a.	-8.24598 kcal/mol		

Table 3: Molecular docking results of compound **2** with CDK-2 enzyme.

S. NO.	**DOCKING STUDY**		
1.	**H-bond interactions**		
	H-bond distance (in angstrom)	**Molecule part involved**	**Active site of Enzyme**
a.	2.57	Amidic -NH	Aspartic acid coil (145)
b.	2.78	Free $-NH_2$ of side chain	β-strand of Leucine (134)
2.	**Best Ligand Pose Energy (Docking energy)**		
a.	-8.6059 kcal/mol		

Table 4: Molecular docking results of compound **3** with CDK-2 enzyme.

S. NO.	**DOCKING STUDY**		
1.	**H-bond interactions**		
	H-bond distance (in angstrom)	**Molecule part involved**	**Active site of Enzyme**
a.	2.99	Amidic -C=O	Aspartic acid coil (145)
b.	2.98	Free $-NH_2$ of side chain	Histidine (84)
c.	2.92	-NH of side chain	β-strand of Leucine (83)
d.	2.71	Free $-NH_2$ of side chain	β-strand of Leucine (83)
2.	**Best Ligand Pose Energy (Docking energy)**		
a.	-8.99135 kcal/mol		

Table 4: Molecular docking results of compound **4** with CDK-2 enzyme.

S. NO.	**DOCKING STUDY**		
1.	**H-bond interactions**		
	H-bond distance (in angstrom)	**Molecule part involved**	**Active site of Enzyme**
a.	2.91	Phenolic -OH	Aspartic acid coil (145)
b.	2.74	Amidic –C=O	Aspartic acid coil (145)
c.	2.85	Amidic -NH	Aspartic acid coil (145)

d.	2.98	Ether linker oxygen	β-strand of Leucine (83)
e.	2.62	Free $-NH_2$ of side chain	β-strand of Leucine (83)
2.	**Best Ligand Pose Energy (Docking energy)**		
a.	-10.8251 kcal/mol		

Table 5: Molecular docking results of compound **5** with CDK-2 enzyme.

S. NO.	**DOCKING STUDY**		
1.	**H-bond interactions**		
	H-bond distance (in angstrom)	**Molecule part involved**	**Active site of Enzyme**
a.	2.46	Free $-NH_2$ of side chain	Glutamine (131)
b.	2.19	Amidic –NH	Glutamic acid (81)
c.	2.21	Phenolic –OH	β-strand of Leucine (83)
d.	2.55	Amidic –C=O	β-strand of Leucine (83)
2.	**Best Ligand Pose Energy (Docking energy)**		
a.	-10.505 kcal/mol		

Table 6: Molecular docking results of compound **6** with CDK-2 enzyme.

S. NO.	**DOCKING STUDY**		
1.	**H-bond interactions**		
	H-bond distance (in angstrom)	**Molecule part involved**	**Active site of Enzyme**
a.	2.99	Free $-NH_2$ of side chain	Asparagine (132)
b.	2.43	Free $-NH_2$ of side chain	Glutamine (131)
c.	2.96	Amidic –C=O	β-strand of Leucine (83)
d.	2.28 and 2.99	Phenolic -OH	β-strand of Leucine (83)
2.	**Best Ligand Pose Energy (Docking energy)**		
a.	-9.72808 kcal/mol		

So according to docking interactions compounds **1** to **6** were showing binding capacity with CDK-2 enzyme and can used as anticancer agents.

III. Experimental

The Molecular docking study was performed on the Argus Lab 4.0.1 version software. In this study first a molecule was designed and taken for energy optimization by using PM_3 method. The molecule was optimized and used for the docking. The docking study was performed with compound and enzyme CDK-2 (PDB Id: 2FVD). The PDB Id was taken from the protein data bank as in pdb format. The 500 number of poses were selected for the docking procedure.

IV. Conclusions

Now according to the docking data it concludes that the compounds**1-6** have good ability to inhibit the activity of CDK-2 enzyme. So the compounds**1-6** can used as CDK-2 inhibitor and as anticancer agent. The physical parameters of compound 1-6 were showing the good lipophilicity.

Acknowledgements

Authors are thankful to M.L.K.P.G. College, Balrampur.

References

[1]. Joshua H. Atkins; Leland J. Gershell, Selective anticancer drugs,Nat. Rev. Drug Discovery. **2002**, 1, 491-492.
[2]. M. Gordaliza, Natural products as leads to anticancer drugs, Clin. Transl. Oncol.**2007**, 9, 767-776.
[3]. M. F. Braña; M. Cacho; A. Gradillas; B. D. P. Teresa; A. Ramos, Intercalators as Anticancer Drugs, Current Pharmaceutical Design. **2001**, 7, 1745-1780.
[4]. C. E. Stecoza; G. M. Nitulescu; C. Draghici; M. T. Caproiu; O. T. Olaru; M. Bostan; M. Mihaila, Synthesis and Anticancer Evaluation of New 1. 3, 4-Oxadiazole Derivatives, Pharmaceuticals. **2021**, 14, 438.
[5]. W. Cui; A. Aouidate; S. Wang; Q. Yu; Y. Li; S. Yuan, Discovering Anticancer Drugs Via Computational Methods, Frontiers in Pharmacology. 2020,doi:10.3389/fphar.2020.00733.
[6]. M. Zhang; L. Zhang; R. Hei; X. Li; H. Cai; X. Wu; Q. Zheng; C. Cai, CDK Inhibitors in Cancer Therapy, An Overview of Recent Development, Am. J. Cancer Res. **2021**, 11, 1913-1935.
[7]. J. Cicenas, K. Kalyan, A. Sorokinas, A. Jatulyte, D. Valiunas, A. Kaupinis; M. Valius, Highlights of the Latest Advances in Research On CDK Inhibitors, Cancers. **2014**, 6, 2224-2242.
[8]. G. I. Shapiro, Cyclin-Dependent Kinase Pathways As Targets for Cancer Treatment, Journal of Clinical Oncology. **2006**, 24, 1770-1783.
[9]. J. Cicenas; M. Valius, The CDK inhibitors in cancer research and therapy, J. Cancer Res. Clin. Oncol. **2011**, 137, 1409–1418.
[10]. C. S. Martínez; L. M. Gelbert; M. J. Lallena; A. D. Dios,Cyclin dependent kinase (CDK) inhibitors as anticancer drugs, Bioorg. Med. Chem. Lett. **2015**, 25, 3420-3435.
[11]. http://www.arguslab.com