Int. J. Pharm. Investigation, 2025; 15(4):1409-1416.
https://www.jpionline.org

Original Article

In silico and ADMET/Pharmacokinetics Prediction Studies of Some Novel Pyrido-Pyrimidine Derivatives as Anticancer

Pratibha Yadav, Kamal Shah*

Department of Pharmaceutical Chemistry, Institute of Pharmaceutical Research, GLA University, Mathura, Uttar Pradesh, INDIA.

ABSTRACT

Objectives: To investigate the mechanism of pyridopyrimidines derivatives against monopolar spindle1 anticancer target and also predicts the pharmacokinetics parameters involved absorption, distribution, metabolism, elimination and toxicity (ADMET). **Materials and Methods:** One hundred fifty pyridopyrimidines derivatives had been designed and analyzed for drug- likeness. The molecular docking of the entire designed scaffold was performed to protein target. Then the molecular interaction was performed with individual derivative, after that ADMET properties have been predicted. **Results:** Drug-likeness results showed that all the designed pyridopyrimidine derivatives were within the range by Lipinski's rule of five. This study predicted that pyridopyrimidines had potential as an anticancer agent acting via inhibiting MPS-1 target (PDB ID-6H3K). The predicted derivatives which had shown better activity in terms of binding affinity than reference ((palbociclib) were P4, P7, P8 and P13.These compounds had also good ADMET properties. **Conclusions:** Molecular docking and ADMET analyses revealed that pyridopyrimidine derivatives demonstrate promising anticancer potential by effectively targeting MPS1. These compounds engage the MPS1 kinase domain primarily through hydrogen bonds supporting their candidacy as novel MPS1 inhibitors.

Keywords: Cancer, Pyrido-pyrimidines, MPS1, *in silico* study ADME-T/pharmacokinetics etc.

Correspondence:
Prof. Kamal Shah
Institute of Pharmaceutical Research, GLA University, Mathura, Uttar Pradesh, INDIA.
Email: kamal0603@gmail.com

Received: 07-03-2025;
Revised: 26-05-2025;
Accepted: 15-07-2025.

INTRODUCTION

Cancer is one of the second leading causes of death worldwide because the high expenditure on anticancer drugs becomes a burden on public health (Luo *et al.*, 2023). Cancer can occur due to gene mutation and carcinogenic agents that influence the metabolism and change the normal growth pattern of cells (Kurniawan *et al.*, 2021). In many developed countries, the number of deaths is increasing day by day due to a lack of effective treatment (Wang *et al.*, 2021). According to the WHO report, global death due to cancer recorded in 2020 reached 9.90 million; out of this, 5.53 million were men and 4.43 million were women. The number of new cases of breast cancer has reached around 2.26 million (Arruebo *et al.*, 2011; Chawla and Vaidya, 2025). Therefore, breast cancer has replaced lung cancer as the most common in type of cancer in the world (Bai *et al.*, 2023). The research of anticancer medicine is needed because the suffering and number of death cases are unstoppable till now. Cancer treatment is one of the most challenging research areas in the medicinal and pharmacological fields (Brunner, 2016). Currently; there are more than 200 drugs under clinical use. All anticancer drugs are classified into two categories: target-based and toxicity-based agents. Recently, pyridopyrimidine derivatives are under clinical trial and approved for treatment of different kinds cancer, such as chronic myelogenous leukemia, CDK4/CDK6 inhibitors, MEK allosteric site inhibitors and amino pyridopyrimidine as inhibitors of cellular proliferation (YadavandShah, 2022). The resistance is a major concern for cancer patients and a challenge for cancer research scientists (Abourehab *et al.*, 2022). Recently, targeting the cell cycle and mitosis process is an alternative therapeutic strategy for cancer treatment (Dominguez-Brauer *et al.*, 2015). Monopolar spindle-1 is one of the most important targets of protein kinase responsible for regulating the various steps in mitosis, centrosomes, and several different signaling pathways (Yang *et al.*, 2019; Sflakidou *et al.*, 2024; Kang *et al.*, 2007). MPS-1 is overexpressed in numerous types of cancer, such as breast cancer (Daniel *et al.*, 2011; Lee *et al.*, 2013), thyroid cancer (He *et al.*, 2015), pancreatic cancer (Tannous *et al.*, 2013; Skoulidis *et al.*, 2022), glioblastoma (Kitajima *et al.*, 2022), lung cancer (Maciejowski *et al.*, 2010), and its role in neuroblastoma is still unknown. MPS1 is involved in the regulation of chromosome alignment during metaphase along with checkpoint function (Fabritius *et al.*, 2024). Therefore, so many MPS1 inhibitors have been developed and shown anticancer activity, but safety has not reported that is

DOI: 10.5530/ijpi.20250577

why no MPS1 inhibitors have been entered into clinical testing in cancer patients. (Sugimoto *et al.*, 2017) We are investigating the development of more effective anticancer agents by using concepts of computational chemistry, such as computer-aided drug design that could save time and the cost of synthesis for discovering new drug candidates (Pugh *et al.*, 2022). Molecular docking is one of the tools that predict the binding affinity and best binding poses of a molecule with the target (MPS1) (Xing *et al.*, 2021). We explored the design of pyridopyrimidine derivatives based on *in silico* virtual screening for an efficient method for drug development research (Hua *et al.*, 2024). This study examined the design of pyridopyrimidine derivatives, ADMET prediction, and binding potential against MPS1.

MPS1 is an important regulator of facilitate massisive chromosome mis segregation during mitosis with subsequent reentry to G1 phase (Shakya *et al.*, 2024; Gurjar, 2024) MPS1 have properties of activating cGAS-STING signaling in proliferating KL cell and facilitate tumor suppressive function.

The present work aims to explore the potential drug candidates against MPS1 to control the growth of abnormal cancer cells. The molecular docking analysis with the PyRx virtual screening tool was performed against MPS1. Moreover, ADMET analysis was performed for pyridopyrimidine derivatives to evaluate physicochemical, drug-likeness, lipophilicity, toxicity, and pharmacokinetic attributes inside the biological system using Protox-III and the Swiss ADME web server. PROTOX-III is a computational technique for predicting the toxicity of small molecules by analyzing their similarity to toxic substances and structural characteristics. PkCSM helps to predict pharmacokinetic features and drug metabolism, whereas Swiss ADME predicts ADME-T properties like lipophilicity and drug-likeness.

MATERIALS AND METHODS

Molecular docking studies

Legands preparation

A total 150 molecules designed and their structure was drawn through CS Chem Draw Ultra and saved in the mol files format. (YadavandShah, 2021) The structure of standard drug (palbociclib) was taken from Pub Chem database (https://pubchem.ncbi.nlm.nih.gov). All compounds were transferred to PyRx virtual screening tool by using Open Babel one by one then minimized energy and converted into auto-dock ligand pdbqt files format.

Gride preparation

The receptor gride was used to define the specific region of interaction of protein and ligand molecules. This tool was used to determine the region surrounding the active center based on x, y and z coordinate measurements. The resolution of the grid box was centered on the coordinates 5.83, 43.43, and 23.22, which corresponded to the x, y and z axis respectively.

Protein preparation

The crystal structure of target protein that is MPS1 (Monopolar spindle1) (PDB ID-6H3K) was downloaded from the Research Collaboratory for structure bioinformatics Protein Data Bank (RCSB PDB). The protein structure was prepared for docking by removal of water molecules and co-crystallized ligand; the polar hydrogen atom was added and file saved in the pdbqt format.

Molecular docking

For molecular docking, PyRx virtual screening tool (autodock vina) version 8.0 was used. A maximum of ten confirmations were set for each compound using (genetic logarithm) lamarckian, 3D prediction of obtained result. Discovery studio client 2021 was used for visualization of 2D and 3D interaction of docked molecules and protein target. All of the ligands were docked independently, lip dock score was used for analyze various poses of all ligands.

Docking calculation

For docking calculation, discovery studio client 2021 software was used. The target protein MSP1 followed by (PDB ID 6H3K) and resolution of this protein was 2.8A°. On the basis of lowest score of binding energy, the top ranked conformations under gone for visualization and atomic level interaction investigation.

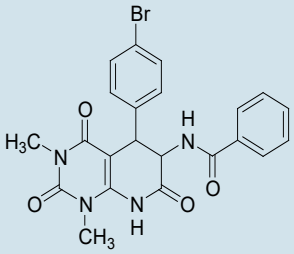
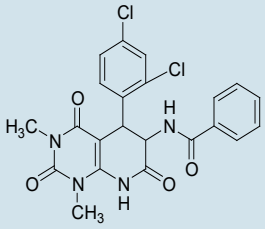
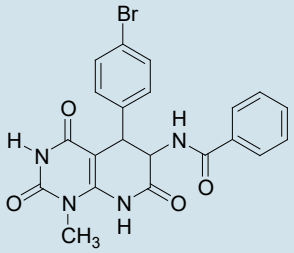
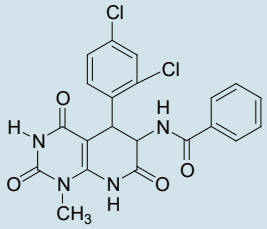
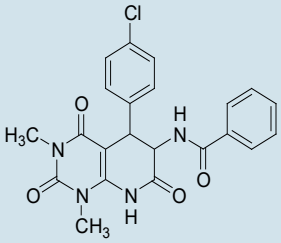
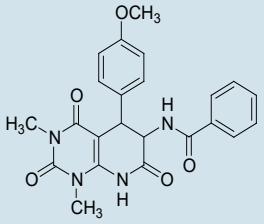
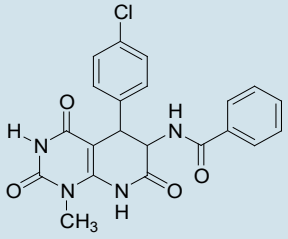
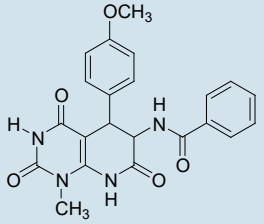
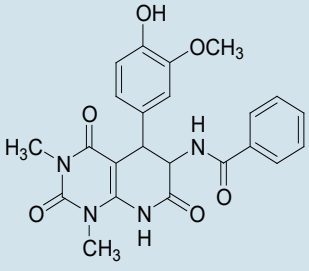
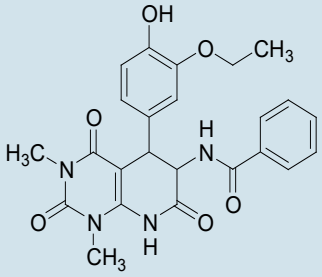
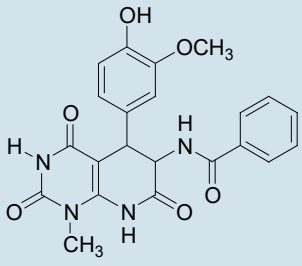
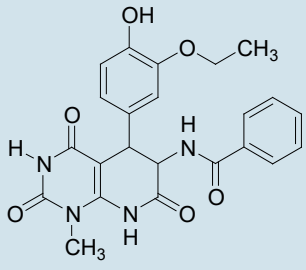
ADMET prediction

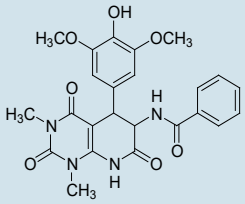
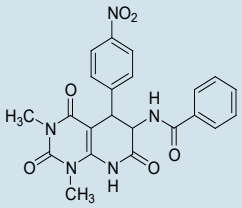
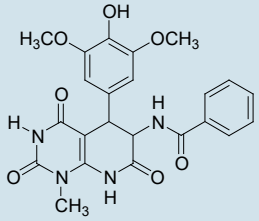
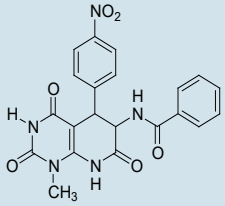
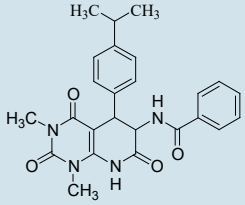
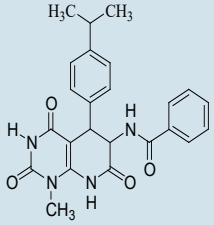
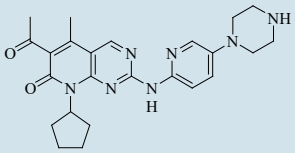
The ADMET analysis of the 150 compounds was screened by using three different web servers for analysis of important pharmacokinetics parameters. The web servers are as follows, https://lmmd.ecust.edu.cn/admetsar2, https://biosig.lab.uq.edu.au/pkcsm/prediction_single/adme http://www.swissadme.ch/, and https://tox.charite.de/protox3/. The descriptors such as molecular weight, hydrogen bond donors, hydrogen bond acceptors, QclogPo/w, QlogS, HIA, BBB permeability, GI absorption and lipinski's rule five (Daina *et al.*, 2017) Based on this result, we selected all compounds for the molecular docking study.

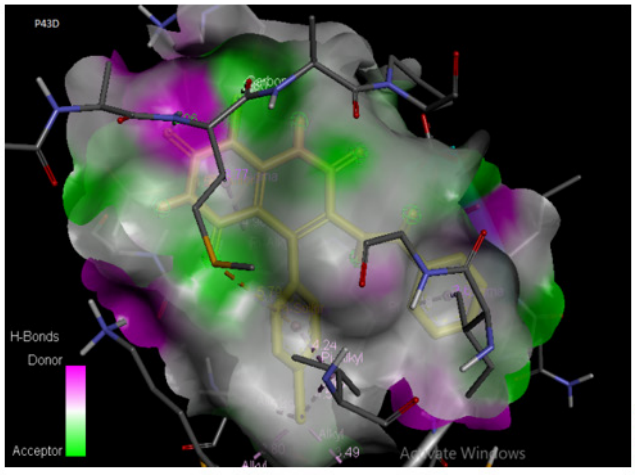
RESULTS

Consequently, these compounds might have a favorable pharmacokinetics profile based on prediction of the ADMET characteristics (Tables 1 and 2). All 150 molecules were screened for using docking studies to identify the most effective pyridopyrimidine bioactive anticancer agents. The top 18 molecules were identified from all of them based on binding energy and hydrogen bonding. The detail of all compounds, the evaluation of the molecular level of interaction showed (Table 3) that the designed scaffold can bind with amino acid residues present in the receptor active domain. The binding pose view of

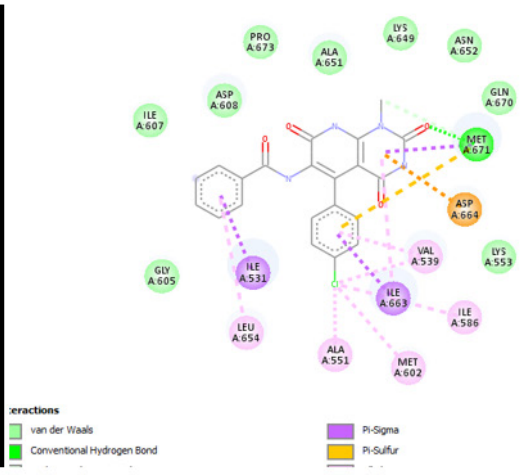
Table 1: Chemical Structure of the 18 Selected Pyrido-pyrimidine derivatives.

Compound code	Molecular structure	Compound code	Molecular structure
P1		P5	
P2		P6	
P3		P7	
P4		P8	
P9		P13	
P10		P14	

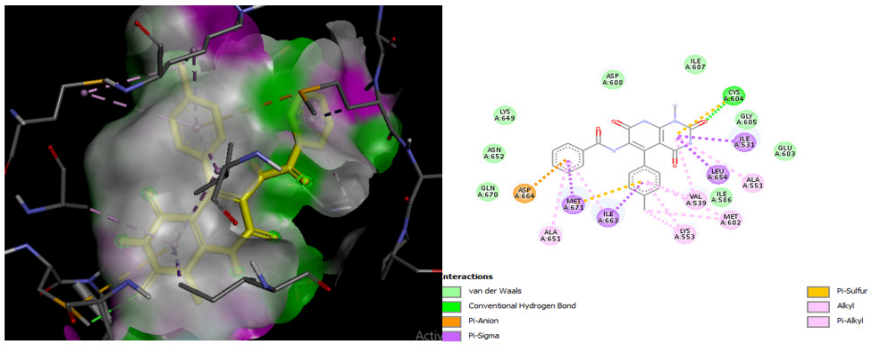
Compound code	Molecular structure	Compound code	Molecular structure
P11		P15	
P12		P16	
P17		P18	
Control (Palbociclib)			



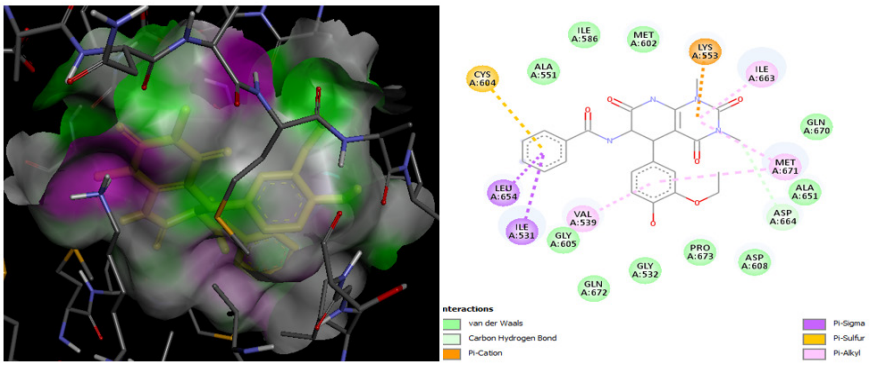
P4 3D



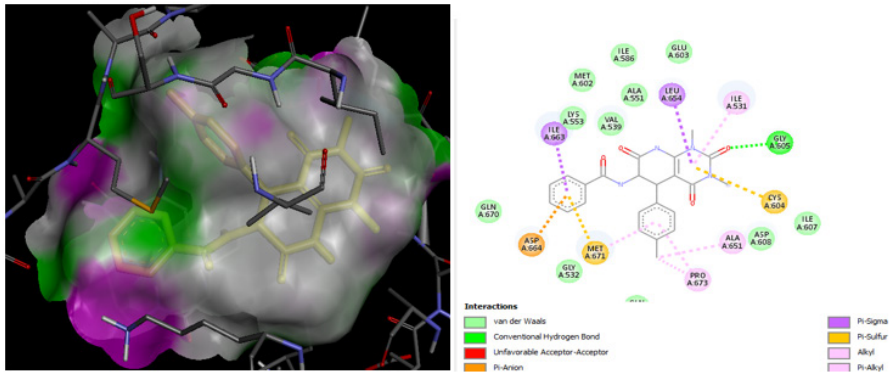
P4 2D



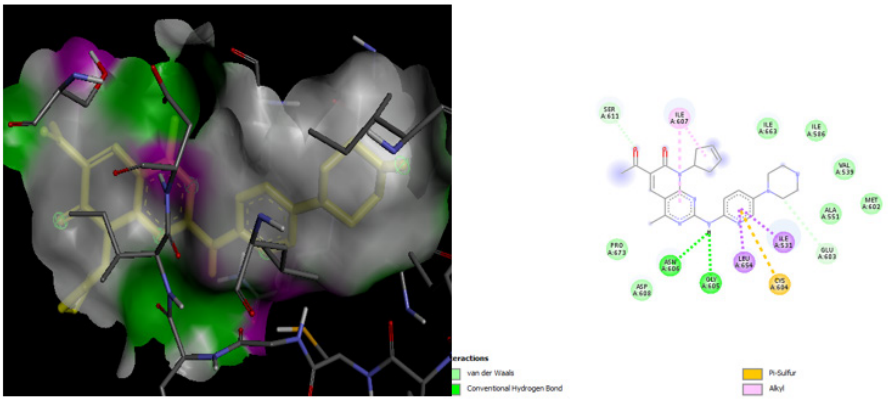
P8 3D **P8 2D**



P13 3D **P13 2D**



P7 3D **P7 2D**



Control 3D **Control 2D**

Figure 1: 3D and 2D interaction poses of lowest binding molecules with MPS-1(PDB ID-6H3K).

Table 2: Docking scores and *in silico* ADME prediction data of the pyridopyrimidines derivatives (P1-P18) with MPS 1(PDBID- 6H3K).

Sl. No.	Code No	Binding score(kca/mol) 6H3K	Rotatable bond	GI absorption	BBB permeability	P-gp substrate	CYP3A4 inhibitors	Log kp (cm/s)	Log S solubility	B S[a]	S A[b]	Toxicitypridiction (Pro-tox-3.0 software)	
												Carcinigenecit	Mutagenicity
1	P1	-6.7	4	High	No	No	Yes	-7.82	-4.27	0.55	4.04	No	No
2	P2	-8.0	4	High	No	Yes	Yes	-7.87	-4.8	0.55	3.89	No	No
3	P3	-7.1	4	High	No	Yes	Yes	-7.60	-3.95	0.55	4.02	No	No
4	P4	-9.7	4	High	No	Yes	Yes	-7.64	-3.76	0.55	3.87	No	No
5	P5	-9.1	4	High	No	No	Yes	-7.66	-3.66	0.55	4.13	No	No
6	P6	-9.7	4	High	No	Yes	Yes	-7.70	-3.47	0.55	3.98	No	No
7	P7	-8.7	4	High	No	Yes	Yes	-7.36	-4.55	0.55	4.14	No	No
8	P8	-6.8	4	High	No	Yes	Yes	-7.40	-4.36	0.55	3.99	No	No
9	P9	-8.1	5	Low	No	Yes	No	-8.23	-3.42	0.55	4.13	No	No
10	P10	-7.0	5	Low	No	Yes	No	-8.27	-3.23	0.55	3.99	No	No
11	P11	-6.9	5	High	No	Yes	Yes	-7.29	-4.22	0.55	4.39	No	No
12	P12	-7.2	5	High	No	Yes	Yes	-7.33	-4.03	0.55	4.2	No	No
13	P13	-9.2	6	Low	No	Yes	Yes	-8.21	-3.53	0.55	4.34	No	No
14	P14	-6.6	6	Low	No	Yes	Yes	-8.26	-3.34	0.55	4.19	No	No
15	P15	-6.9	6	Low	No	Yes	Yes	-8.59	-3.37	0.55	4.39	No	No
16	P16	-6.6	6	High	No	Yes	No	-8.63	-3.18	0.55	4.24	No	No
17	P17	-6.6	5	High	No	Yes	No	-8.39	-3.29	0.55	4.22	No	No
18	P18	-8.6	5	Low	No	Yes	No	-8.43	-3.1	0.55	4.07	No	No
Control	palbociclib	-7.9	5	High	No	Yes	Yes	-7.74	-3.78	0.55	3.57	No	No

Best lowest binding energy – Green colour

Table 3: Analysis of molecular level interaction of molecules shows (lowest binding energy) with MPS-1.

Code of compounds	PDB ID	H Bond interaction	Hydrophobic interaction
P4	6H3K	MET A 671, ASP A 664	ILE A531, LEU A 654, ALA A551, MET A 602, VAL A 539, ASP A 664, ILE A 663
P7		GLY A 605, CYS A 604, MET A 671	PRO A 673, ALA A 651, ILE A 531, ILE A 664, ILE A 663, ASP A 664, ILE A 531
P8		CYS A 604, ASP A 664	ALA A 651, MET A 673, ILE A 663, LYS A 553, MET A 602, LEU A 654, ILE A 532
P13		ASP A 664, CYS A 604	LEU A 654, ILE A 531, VEL A 531, LYS A 553, ILE A 663, MET A 671, ASP A 664
Control (palbociclib)		ASN A 606, GLY A 605	LEU A 654, ILE A 531, CYS A 604

the selected molecules is depicted in Figure 1. but all of them, the docking results showed that P7 had the highest binding score (-9.7kcal/mol).

Against MPS1. Docking analysis of pyridopyrimidine with MPS1 showed that strong molecular interaction such as hydrogen and hydrophobic bonding with amino acids GLY A 605, CYS A 604, MET A 671, PRO A 673, ALA A 651, ILE A 531, ILE A 664, ILE A 663, ASP A 664, ILE A 531 (Figure 1). Still, detailed studies are required to understand the binding activity further. Based on this work, more research could be done to develop new drug candidate that greatly help to treat cancer.

DISCUSSION

All the designed pyrido-pymidines derivatives have wide range of medicinal and pharmacological importance in the area of research. Drug discovery and development process is an expensive and time taken phenomenon. The molecular docking and ADME-T analysis will help to identity potential drug candidate before going experimental procedure, this techniques will reduce time and man power required for synthesis of millions of molecules and wastage of chemicals. The ADME-T and drug-likeness prediction of all our designed pyridopyrimidines had investigated by using rotox-III, pkCSM, and the SwissADME web server. Based on the determined value, the maximum of compounds

Table 4: *In silico* evaluation of Lipinski's rule of five and physicochemical characteristics of pyridopyrimidine derivatives (P1-P18).

Lipinski rule of five and physicochemical properties							
Descriptors		MW	HBD	HBA	cLogPo/w	No of rule violation	druglikeness
Sl. No.	Code No	≤500 Dalton	≤5	≤10	≤5	≤ 2 violations	
1	P1	483.31	2	4	2.91	0	Yes
2	P2	469.29	3	4	2.36	0	Yes
3	P3	438.86	2	4	2.84	0	Yes
4	P4	424.84	3	4	2.19	0	Yes
5	P5	418.45	2	4	2.78	0	Yes
6	P6	404.42	3	4	2.05	0	Yes
7	P7	473.31	2	4	3.02	0	Yes
8	P8	459.28	3	4	2.23	0	Yes
9	P9	449.42	2	6	2.36	1	Yes
10	P10	435.39	3	6	1.93	1	Yes
11	P11	446.5	2	4	2.81	0	Yes
12	P12	432.47	3	4	2.7	0	Yes
13	P13	464.42	3	6	2.81	0	Yes
14	P14	450.44	4	6	2.62	0	Yes
15	P15	480.47	3	7	2.95	1	Yes
16	P16	466.44	4	7	2.36	1	Yes
17	P17	450.44	3	6	2.54	0	Yes
18	P18	436.42	4	6	2.01	0	Yes
Control	Palbociclib	447.53	2	6	2.23	1	Yes

showed all descriptors of Lipinski rule of five, mention detailed in Table 4. The primary factors of significance are the molecular weight below 500 Daltons and log *p* value ranged from (1.93 to 3.02) indicates that passive intestinal absorption. The ADMET parameter is crucial for lipophilicity and capacity to cross critical biological barrier and membranes. Remember, if molecules with high lipophilicity show poor solubility, affecting bioavailability or accumulate in adipose tissues cause slow excretion and influences systemic toxicity. An important determinant oral bioavailability depends on total number of hydrogen donors and hydrogen acceptors. The calculated all parameters for all tested compounds came under standards limits.

CONCLUSION

In this research work, we designed all 150 different derivatives of Pyrido-pyrimidines motifs but we are showing best docked score of 18 compounds and evaluated their molecular docking studies with receptor for anti-cancer activity through *in silico* studies. All of the compounds in this series showed favorable pharmacokinetic properties such as Absorption, Distribution, Metabolism, Elimination, and Toxicity (ADME-T). According to docking studies, substances P4, P7, P8, and P13 exhibited the highest binding affinities when compared to palbociclib (with mono-polar spindle-1 (PDB ID-6H3K)). Docking and ADMET studies demonstrated that these ligands interacted mostly with the MPS1 receptor for anticancer reports by forming hydrogen bonds and interacting hydrophobically with the domain. The above study signifies if the suggested compounds screened. They may have promising anticancer activity.

ACKNOWLEDGEMENT

The authors are thankful for the immense support of the institute of Pharmaceutical Research, GLA University, Mathura, Utter Pradesh, India.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

WHO: World health organization; **MPS-1:** Monopolar splindle-1; **MW:** Molecular weight; **HBD:** Hydrogen bond donar; **HBA:** Hydrogen bond acceptor; **ADME:** Absorption distribution metabolism and elimination; **BBB:** Blood brain barrier; **PDB:** Protein data bank etc.

REFERENCES

Abourehab, M. A. S., Alqahtani, A. M., Almalki, F. A., Abdalla, A. N., & Gouda, A. M. (2022). Pyrrolizine/indolizine-cinnamaldehyde Schiff bases: Design, synthesis, biological evaluation, ADME, and molecular docking study. European Journal of Medicinal Chemistry Reports, 4, Article 100036. https://doi.org/10.1016/J.EJMCR.2022.100036

Arruebo, M., Vilaboa, N., Sáez-Gutierrez, B., Lambea, J., Tres, A., Valladares, M., & González-Fernández, A. (2011). Assessment of the evolution of cancer treatment therapies. Cancers, 3(3), 3279–3330. https://doi.org/10.3390/CANCERS3033279

Bai, Y., Aodeng, G., Ga, L., Hai, W., & Ai, J. (2023). Research progress of metal anticancer drugs. Pharmaceutics, 15(12), 2750. https://doi.org/10.3390/PHARMACEUTICS15122750

Brunner, T. B. (2016). The rationale of combined radiotherapy and chemotherapy-Joint action of Castor and Pollux. Best Practice and Research. Clinical Gastroenterology, 30(4), 515–528. https://doi.org/10.1016/J.BPG.2016.07.002

Chawla, R., & Vaidya, A. (2024). Anticancer mechanism of quinoline based compounds for cancer therapy. International Journal of Medical, Pharmaceutical and Health Sciences, 1(2), 65–79. https://doi.org/10.62946/IJMPHS/1.2.65-79

Daina, A., Michielin, O., & Zoete, V. (2017). SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Scientific Reports, 7(1), Article 42717. https://doi.org/10.1038/srep42717

Daniel, J., Coulter, J., Woo, J.-H., Wilsbach, K., & Gabrielson, E. (2011). High levels of the Mps1 checkpoint protein are protective of aneuploidy in breast cancer cells. Proceedings of the National Academy of Sciences of the United States of America, 108(13), 5384–5389. https://doi.org/10.1073/pnas.1007645108

Dominguez-Brauer, C., Thu, K. L., Mason, J. M., Blaser, H., Bray, M. R., & Mak, T. W. (2015). Targeting mitosis in cancer: Emerging strategies. Molecular Cell, 60(4), 524–536. https://doi.org/10.1016/J.MOLCEL.2015.11.006

Fabritius, A., Alonso, A., Wood, A., Sulthana, S., & Winey, M. (2024). Spindle checkpoint activation by fungal orthologs of the S. cerevisiae Mps1 kinase. PLOS One, 19(3), Article e0301084. https://doi.org/10.1371/JOURNAL.PONE.0301084

Gurjar, V. K. (2024). Recent advances in oxygen-containing heterocycles as anticancer agents. International Journal of Medical, Pharmaceutical and Health Sciences, 1(2), 80–93. https://doi.org/10.62946/IJMPHS/1.2.80-93

He, Y., Meng, Z., Jia, Q., Hu, F., He, X., Tan, J., Zhang, G., Li, X., Zhang, J., Zhang, Q., Liu, L., Zhao, L., Li, J., Wang, Y., Qian, Y., Hou, S., Liu, H., Wang, S., Wang, R., (2015). Sleep quality of patients with differentiated thyroid cancer. PLOS One, 10(6), Article e0130634. https://doi.org/10.1371/journal.pone.0130634

Hua, H., Guan, L., Pan, B., Gao, J., Geng, Y., Niu, M.-M., Li, Z., & Li, J. (2024). The identification of potent dual-target monopolar spindle 1 (MPS1) and histone deacetylase 8 (HDAC8) inhibitors through pharmacophore modeling, molecular docking, molecular dynamics simulations, and biological evaluation. Frontiers in Pharmacology, 15, Article 1454523. https://doi.org/10.3389/FPHAR.2024.1454523

Kang, J., Chen, Y., Zhao, Y., & Yu, H. (2007). Autophosphorylation-dependent activation of human Mps1 is required for the spindle checkpoint. Proceedings of the National Academy of Sciences of the United States of America, 104(51), 20232–20237. https://doi.org/10.1073/pnas.0710519105

Kitajima, S., Tani, T., Springer, B. F., Campisi, M., Osaki, T., Haratani, K., Chen, M., Knelson, E. H., Mahadevan, N. R., Ritter, J., Yoshida, R., Köhler, J., Ogino, A., Nozawa, R.-S., Sundararaman, S. K., Thai, T. C., Homme, M., Piel, B., Kivlehan, S., (2022). MPS1 inhibition primes immunogenicity of KRAS-LKB1 mutant lung cancer. Cancer Cell, 40(10), 1128–1144.e8. https://doi.org/10.1016/J.CCELL.2022.08.015

Kurniawan, Y. S., & Priyangga, K. T. A., Jumina, Pranowo, H. D., Sholikhah, E. N., Zulkarnain, A. K., Fatimi, H. A., and Julianus, J. (2021). An Update on the Anticancer Activity of Xanthone Derivatives: A Review. Pharmaceuticals 2021, Vol. 14, Page 1144, 14(11), 1144. https://doi.org/10.3390/PH14111144.

Lee, J., Hwang, J.-A., & Lee, E. K. (2013). Recent progress of genome study for anaplastic thyroid cancer. Genomics and Informatics, 11(2), 68–75. https://doi.org/10.5808/GI.2013.11.2.68

Luo, X., Du, X., Huang, L., Guo, Q., Tan, R., Zhou, Y., Li, Z., Xue, X., Li, T., Le, K., Qian, F., Chow, S.-C., & Yang, Y. (2023). The price, efficacy, and safety of within-class targeted anticancer medicines between domestic and imported drugs in China: A comparative analysis. The Lancet Regional Health. Western Pacific, 32, Article 100670. https://doi.org/10.1016/J.LANWPC.2022.100670

Maciejowski, J., George, K. A., Terret, M.-E., Zhang, C., Shokat, K. M., & Jallepalli, P. V. (2010). Mps1 directs the assembly of Cdc20 inhibitory complexes during interphase and mitosis to control M phase timing and spindle checkpoint signaling. The Journal of Cell Biology, 190(1), 89–100. https://doi.org/10.1083/JCB.201001050

Pugh, L., Pancholi, A., Purat, P. C., Agudo-Alvarez, S., Benito-Arenas, R., Bastida, A., & Bolanos-Garcia, V. M. (2022). Computational biology dynamics of Mps1 kinase molecular interactions with isoflavones reveals a chemical scaffold with potential to develop new therapeutics for the treatment of cancer. International Journal of Molecular Sciences, 23(22), Article 14228. https://doi.org/10.3390/IJMS232214228

Sflakidou, E., Adhikari, B., Siokatas, C., Wolf, E., & Sarli, V. (2024). Development of 2-aminoadenine-based proteolysis-targeting chimeras (PROTACs) as novel potent degraders of monopolar spindle 1 and Aurora kinases. ACS Pharmacology and Translational Science, 7(11), 3488–3501. https://doi.org/10.1021/ACSPTSCI.4C00405

Shakya, R., Priya, S., Kasana, S., Islam, M. M., Kurmi, B. D., & Patel, P. (2024). Exploring the binding modes of Quinazolinone-1, 2, 4-Triazole Hybrids on PARP-10 Inhibition for Anti-Neoplastic Therapy: Docking and ADME Studies. International Journal of Medical Pharmaceutical and Health Sciences, 141–152.

Skoulidis, F., Heymach, J. V., & Cascone, T. (2022). A STING operation to expose KRAS and STK11 co-mutated lung cancers. Cancer Cell, 40(10), 1073–1076. https://doi.org/10.1016/J.CCELL.2022.09.010

Sugimoto, Y., Sawant, D. B., Fisk, H. A., Mao, L., Li, C., Chettiar, S., Li, P.-K., Darby, M. V., & Brueggemeier, R. W. (2017). Novel pyrrolopyrimidines as Mps1/TTK kinase inhibitors for breast cancer. Bioorganic and Medicinal Chemistry, 25(7), 2156–2166. https://doi.org/10.1016/J.BMC.2017.02.030

Tannous, B. A., Kerami, M., Van Der Stoop, P. M., Kwiatkowski, N., Wang, J., Zhou, W., Kessler, A. F., Lewandrowski, G., Hiddingh, L., Sol, N., Lagerweij, T., Wedekind, L., Niers, J. M., Barazas, M., Nilsson, R. J. A., Geerts, D., De Witt Hamer, P. C., Hagemann, C., Vandertop, W. P., (2013). Effects of the selective MPS1 inhibitor MPS1-IN-3 on glioblastoma sensitivity to antimitotic drugs. Journal of the National Cancer Institute, 105(17), 1322–1331. https://doi.org/10.1093/JNCI/DJT168

Wang, J., Tao, J., Jia, S., Wang, M., Jiang, H., & Du, Z. (2021). The protein-binding behavior of platinum anticancer drugs in blood revealed by mass spectrometry. Pharmaceuticals, 14(2), 104. https://doi.org/10.3390/PH14020104

Xing, C., Zhou, X., Chen, C., Sun, W., Zheng, Q., & Liang, D. (2021). Studies of interaction mechanism between pyrido [3,4-d] pyrimidine inhibitors and Mps1. Molecules, 26(16), 5075. https://doi.org/10.3390/molecules26165075, 26(16), 5075

Yadav, P., & Shah, K. (2021). An overview on synthetic and pharmaceutical prospective of pyrido[2,3-d]pyrimidines scaffold. Chemical Biology and Drug Design, 97(3), 633–648. https://doi.org/10.1111/CBDD.13800

Yadav, P., & Shah, K. (2022). Chemistry and biological evaluation of pyrido [4, 3-d] pyrimidines: A review. Chemical Biology and Drug Design, 99(5), 758–768. https://doi.org/10.1111/cbdd.14026

Yang, H., Zhang, F., Huang, C.-J., Liao, J., Han, Y., Hao, P., Chu, Y., Lu, X., Li, W., Yu, H., & Kang, J. (2019). Mps1 regulates spindle morphology through MCRS1 to promote chromosome alignment. Molecular Biology of the Cell, 30(9), 1060–1068. https://doi.org/10.1091/mbc.E18-09-0546.

Cite this article: Yadav P, Shah K. *In silico* and ADMET/Pharmacokinetics Prediction Studies of Some Novel Pyrido-Pyrimidine Derivatives as Anticancer. Int. J. Pharm. Investigation. 2025;15(4):1409-16.