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Original Article

Evaluating the Therapeutic Potential of Duartin against Aurora A Protein Kinase in Breast Cancer Cells

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ABSTRACT

Background: Cancer, particularly breast cancer, remains a major global health challenge, prompting ongoing research into novel therapeutic targets. This study focuses on Aurora A protein kinase, a serine/threonine kinase crucial for mitotic regulation, which is often overexpressed in various cancers, as well as breast cancer. **Materials and Methods:** Recent study was aimed to explore the inhibitory potential of Duartin, a plant-derived isoflavonoid, against Aurora A protein kinase. Using molecular docking studies, Duartin demonstrated a high binding affinity with Aurora A, forming stable interactions with key residues, suggesting its potential as a strong inhibitor. ADMET predictions, along with PASS and Swiss Target Prediction analyses, confirmed Duartin's favorable drug-like belongings, including effective absorption, distribution, metabolism, and low toxicity. **Results:** *In vitro* assays on MDA-MB-231 breast cancer cells revealed significant cytotoxic effects of Duartin, by means of an IC_{50} value of 13.42 µM. Additionally, time-dependent cytotoxicity assays showed sustained reduction in cell viability over 48 hr. Furthermore, treatment with Duartin significantly reduced the mRNA expression levels of Aurora A protein kinase in these cells, indicating potent inhibitory effects on its gene expression. The findings suggest that Duartin not only exhibits strong binding affinity and favourable ADMET properties but also effectively reduces cell viability and Aurora A protein kinase expression in breast cancer cells. **Conclusion:** The outcomes of this investigation highlights Duartin's potential as a promising therapeutic agent for breast cancer, warranting further preclinical and clinical investigations.

Keywords: ADMET predictions, Aurora A protein kinase, Breast cancer, Cytotoxic effects, Duartin, Molecular docking.

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INTRODUCTION

In 2020 alone, an estimated 19.3 million new cases and 10 million deaths from cancer were reported, making it one of the most serious health issues in the globe (Sung *et al*., 2021). Despite advancements in early detection, diagnostic techniques and treatment modalities, the high mortality rate and the significant burden of disease necessitate continuous exploration for novel therapeutic targets and strategies (Liu *et al*., 2024). One of the promising avenues in cancer therapy is the targeting of specific molecular pathways that are dysregulated in cancer cells, principal to uncontrolled proliferation and survival. Among these, protein kinases have emerged as critical regulators of cell signalling and are thus attractive targets for cancer therapy (Bhullar *et al*., 2018).

Aurora kinases, a family of serine/threonine kinases, show a essential role in the regulation of mitosis (Fu *et al*., 2007). They ensure proper chromosome alignment, segregation and cytokinesis, thus maintaining genomic stability (Roshan *et al*., 2023). This family comprises three members: Aurora A, Aurora B and Aurora C, each with distinct yet overlapping functions during cell division (Willems *et al*., 2018). Aurora Several crucial processes in mitosis, such as spindle formation, chromosomal alignment, and centrosome maturation and separation, depend on a kinase in particular (Magnaghi-Jaulin *et al*., 2019).

Overexpression and hyperactivation of Aurora A have been frequently observed in various cancers, including breast (Ingebriktsen *et al*., 2024), hepatocellular (Jeng *et al*., 2004), esophageal squamous cell carcinoma (Wang *et al*., 2006), head and neck (Mehra *et al*., 2013), and pancreatic cancers (Zhang *et al*., 2022). This aberrant expression correlates with poor prognosis, increased tumor violence, and resistance to conventional therapies (Zhang *et al*., 2004; Zheng *et al*., 2023). As a result, Aurora A kinase has gained significant attention as a potential therapeutic aim in oncology.

Aurora A kinase is located on chromosome 20q13, a region generally amplified in cancers (Keen and Taylor, 2004; Kitzen *et al*., 2010; Sen *et al*., 1997). Its overexpression is associated with

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aneuploidy and chromosomal instability, hallmark features of cancer cells (Takeshita *et al*., 2013). Aurora A contributes to the malignant phenotype by disrupting normal mitotic processes, leading to abnormal centrosome function, spindle assembly defects and improper chromosome segregation (Goldenson *et al*., 2015; Sasai *et al*., 2008). These aberrations result in genomic instability, a driving force behind cancer progression and metastasis (Torchia *et al*., 2009). Moreover, Aurora A interacts with several key oncogenic and tumor suppressor pathways (Lin *et al*., 2020). Aurora A also inactivates the tumor suppressor protein p53 by phosphorylation, leading to impaired DNA damage response and apoptosis (Katayama *et al*., 2012). These interactions determine the role of Aurora A in cancer development and highlight its possible as a therapeutic target.

Targeting the Aurora A kinase presents a promising therapeutic strategy due to its central role in mitosis and cancer pathogenesis. Inhibitors of Aurora A aim to disrupt its kinase activity, thereby inducing mitotic defects, cell cycle arrest, and apoptosis in cancer cells. The development of Aurora A inhibitors, along with combination strategies and novel inhibitors with improved selectivity holds promise for enhancing therapeutic outcomes and overcoming resistance.

MATERIALS AND METHODS

Retrieval and preparation of the target molecule

The crystal structure of human Aurora A protein kinase was downloaded from RCSB PDB database, with PDB ID: 1MQ4 (Nowakowski *et al*., 2002). The structure was prepared using a standard receptor protocol. Swiss-PDB Viewer tools were used to check and correct any structural issues in the protein molecule; such include erroneous bond arrangements or missing atoms, or unresolved residues. Further, energy minimization was performed to repair distorted geometries via moving atoms and releasing internal constraints on the protein structure. Hydrogen atoms and Kollman United Atom Charges were then additional to the structure. Finally, the structure was saved in. pdbqt format using MGLTools.

Retrieval and preparation of the ligand molecules

A small isoflavonoid library of 39 plant-derived natural compounds was curated and docked in contradiction of the target protein. The structures of these ligand molecules were downloaded in mol format and converted to the PDB format using Open Babel tools. Hydrogen atoms were then added to the ligand molecules using PyMOL. Swiss-PDB viewer was employed to carry out energy minimization and relax the ligand structure to its lowest energy conformation. The structure of each ligand molecule was verified for any missing atoms, incorrect bond orders, or other structural issues using molecular modeling software. Appropriate atomic charges were subsequently assigned to the ligand molecules. Finally, the optimized and corrected ligand structures were saved in PDBQT format using MGLTools, which is essential for docking using AutoDock Vina.

Molecular docking

We utilized AutoDock Vina for the molecular docking process, performing blind docking of ligand molecules with the Aurora A protein kinase (Trott *et al*., 2010). The grid dimensions for the X, Y and Z coordinates were set to 67, 83, and 88 Å, respectively, centered at -42.34, 16.21, and 71.13. The grid spacing was fixed at 1.00 Å with an exhaustiveness parameter of 8. Binding affinity was evaluated and the resulting docked complexes were visualized by means of PyMOL and Discovery Studio Visualizer to analyze the interaction patterns between the ligand molecules and the Aurora A protein kinase.

ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) characteristics of Duartin

To assess the ADMET characteristics of a ligand molecule, we utilized online tools such as SwissADME (http://www.swissadme.ch/index.php) and pkCSM (https://biosig.lab.uq.edu.au/pkcsm/). Integrating the results from both SwissADME and pkCSM provides a thorough understanding of the ADMET properties of the top hit.

Swiss Target Prediction tool and PASS online are used to predict Duartin's activity spectrum

This study utilized PASS Online (http://www.pharmaexpert.ru/passonline/) and the Swiss Target Prediction tool (http://www.swisstargetprediction.ch/) to identify the activity spectrum of Duartin. PASS Online (Prediction of Activity Spectra for Substances) is a web-based platform that predicts the biological and pharmacological activities of chemical compounds, helping researchers identify potential activities and properties of small molecules. Swiss Target Prediction is an online program that assists in identifying proteins that might interact with a particular substance by predicting possible targets for small molecules or medications.

Test compound and MDA-MB-231 breast cancer cells

Duartin (>97.0% GC(T)) was obtained from MedKoo Biosciences, Inc. and liquefied in DMSO (SRL) to prepare a stock solution with a concentration of 500 μg/mL. MDA-MB-231 cells were sourced from NCCS, Pune and cultured in DMEM supplemented by means of 10% FBS and 1% antibiotics.

Cell culture and cytotoxicity assay

MDA-MB-231 cells were cultured in DMEM by 10% FBS and 1% penicillin-streptomycin at 37ºC with 5% CO_2 until confluency. The cells were then seeded into 96-well plates at 5,000 cells/well and grown for 48 hr. They were treated by Duartin (0-1000 μM) for 72 hr, with control wells left untreated. Subsequently treatment, 100 μL of 5 mg/mL MTT solution was additional to

each well and incubated at 37ºC for 3-4 hr. The MTT solution was substituted with 100 µL of DMSO to solubilize the formazan crystals, and absorbance was measured at 570 nm (reference at 630 nm). Cell viability (%) was considered as [Absorbance of treated cells/Absorbance of control cells] × 100. Additionally, a time-dependent viability assay was performed at 24, 48, and 72 hr using the IC_{50} concentration of Duartin.

mRNA expression of Aurora A protein kinase in Duartin treated MDA-MB-231 breast cancer cells

Breast cancer cells (MDA-MB-231) were treated with the IC_{50} concentration of Duartin for 48 hr. RNA was taken out using TRIzol Reagent (Thermo Fisher). cDNA was made by using cDNA Synthesis Kit (Almanac, Cat# ALS-MB72). The quantitative qRT-PCR was conducted consuming SYBR Green (Almanac, Cat# ALS-MB76) on an Applied Biosystems RT-PCR System. The 2-ΔΔCT method was working to calculate the relative fold change in gene expression. The primer sequence used for the amplifications was as: Aurora A protein kinase, forward: 5′-CCACCTTCGGCATCCTAATA-3′ and reverse: 5′-TCCAAGTGGTGCATATTCCA-3′ and GAPDH, forward: 5′-GAAGGTGAAGGTCGGAGTC-3′ and reverse: 5′-GAAGATGGTGATGGGATTTC-3′ (Wang *et al.*, 2019).

RESULTS

Molecular docking and ADMET properties

The highest binding affinity was observed between Duartin and the Aurora A protein kinase. The binding affinity results are represented in Table 1 and Figures 1A-C. The interaction patterns of the top five hits are depicted in Figure 1C. Duartin formed several conventional hydrogen bonds with the LYS41 and ALA213 residues of Aurora A protein kinase. Additionally, Duartin formed various other interactions, as well as van der Waals, carbon hydrogen, Pi-sigma, alkyl, and Pi-alkyl bonds, with the LYS143, GLY142, GLY140, GLU260, THR217, GLY216, LEU139, PRO214, TYR212, VAL147, LEU263, LEU210, ALA160, LYS162 and ASP274 residues of Aurora A.

ADMET predictions, PASS analysis and Swiss Target Prediction

ADMET estimates, PASS examination, and SwissTargetPrediction collectively encourage the drug-like characteristic of Duartin. The ADMET properties of Duartin, presented in Table 2, demonstrate favourable characteristics in terms of absorption, distribution, metabolism, excretion, and lack of toxicity. Furthermore, the outcomes of PASS Analysis and SwissTargetPrediction analysis, represented in Table 3 and Figure 2 respectively, not only confirm but also elaborate on the diverse biological properties associated with Duartin.

Concentration-dependent cytotoxic effect of Duartin on breast cancer cells (MDA-MB-231)

The outcomes of the concentration-dependent cell toxicity assay are presented in Figure 3. This assay demonstrated a significant impact of Duartin on the viability of MDA-MB-231 cells. Additionally, the IC_{50} value for Duartin was determined to be 13.42 µM in MDA-MB-231 cancer cells.

Time dependent cytotoxic effect of Duartin on breast cancer cells

The outcomes of the time-dependent cell toxicity assay are depicted in Figure 4. Increased exposure durations of breast cancer cells to the IC_{50} concentration of Duartin significantly impacted their viability for up to 48 hr.

Expression of Aurora A protein kinase in Duartin treated breast cancer cells

The outcomes represented in Figure 5 illustration a statistically significant effect of the IC_{50} concentration of Duartin on the mRNA expression of Aurora A protein kinase in breast cancer cells. Specifically, mRNA expression was significantly reduced ($p<0.001$) in Duartin-treated cells compared to untreated cells.

DISCUSSION

Initially, the study aimed to investigate the binding affinity of various compounds with the Aurora A protein kinase, a crucial enzyme involved in cell cycle regulation and mitotic spindle assembly (Carmena *et al.*, 2009). The results demonstrated that Duartin exhibited the highest binding affinity with Aurora A protein kinase, suggesting its potential as a strong inhibitor of this kinase. The binding affinity indicated that Duartin forms multiple stable interactions with key residues of Aurora A protein kinase. Specifically, Duartin establishes conventional hydrogen bonds with the LYS41 and ALA213 residues, which are critical for the stabilization of the ligand-protein complex (Panigrahi and Desiraju, 2007). The presence of these hydrogen bonds likely contributes significantly to the high binding affinity observed (Chen *et al.*, 2016). Moreover, Duartin also engaged in a diversity of other non-covalent interactions, as well as van der Waals forces, carbon hydrogen bonds, Pi-sigma interactions, alkyl bonds, and Pi-alkyl bonds. These interactions further stabilize the Duartin-Aurora A complex, enhancing the overall binding affinity. The interaction pattern of Duartin with Aurora A protein kinase, emphasize the unique and robust interaction network formed by Duartin. The diverse array of bonds and interactions not only highlights the strong binding capability of Duartin but also highlights its specificity towards Aurora A protein kinase (Pitsawong *et al.*, 2018; Zorba *et al.*, 2014). This specificity is crucial for the development of targeted inhibitors that can effectively disrupt Aurora A protein kinase activity without

Table 1: Binding affinity and interaction of Duartin with Aurora-A protein kinase.

Name of the ligand	Target protein	Binding Energy (kcal/mol)	pKi	Target protein's amino acids interacting with ligand molecules
Duartin	Aurora-A protein kinase.	Aurora-A protein kinase.	5.94	Conventional hydrogen bonds: LYS41, ALA213 van der Waals and other interactions: LYS143, GLY142, GLY140, GLU260, THR217, GLY216, LEU139, PRO214, TYR212, VAL147, LEU263, LEU210, ALA160, LYS162, ASP274.

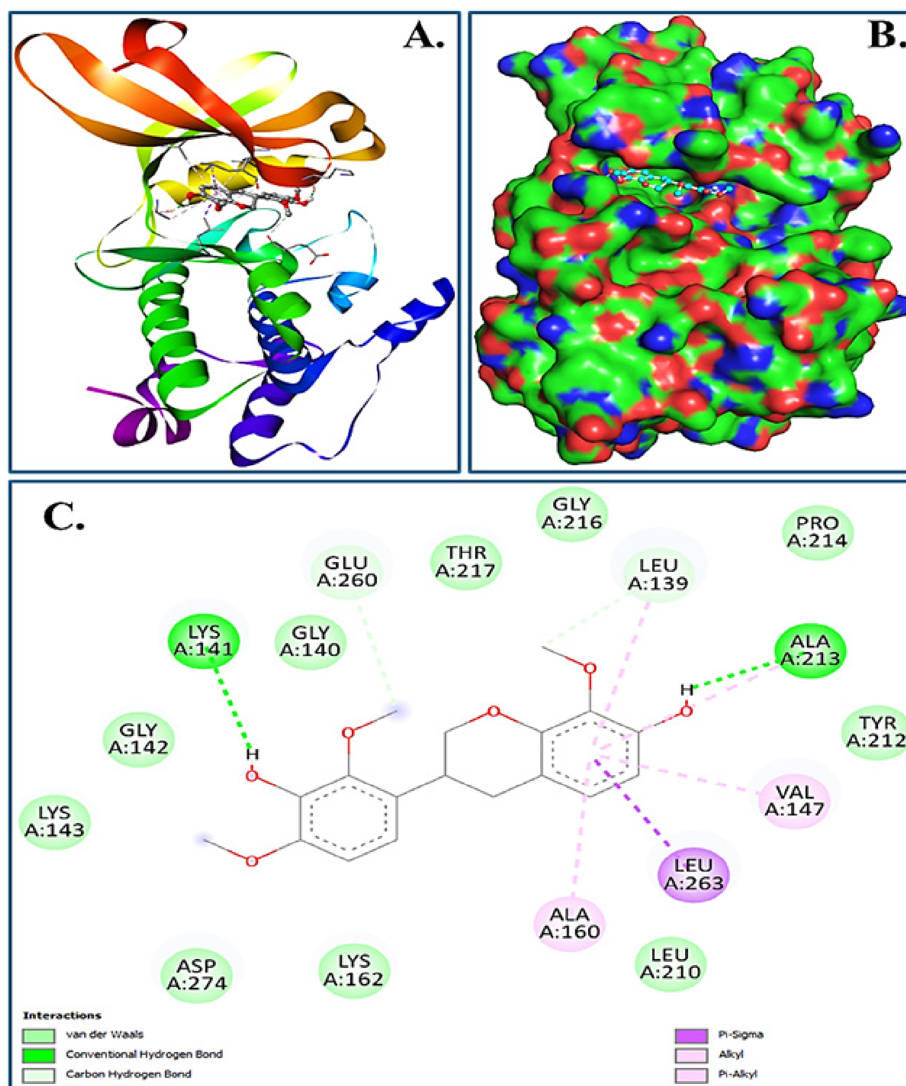


Figure 1: Molecular docking of Duartin with Aurora A protein kinase. (A) Cartoon representation, (B) Surface view representing binding of Duartin within deep groove and (C) 2D docked complex showing interaction of Duartin with various amino acid residues of Aurora A protein kinase.

affecting other kinases, thereby minimizing potential off-target effects (Zorba *et al*., 2014).

The findings of this study provide a comprehensive evaluation of the drug-like properties of Duartin, supported by ADMET calculations, PASS examination, and Swiss Target Prediction. The ADMET properties direct that Duartin keeps promising features in terms of absorption, distribution, metabolism, and excretion, while also exhibiting a lack of toxicity. These properties are crucial for any potential therapeutic agent, as they ensure that the compound can be efficiently absorbed, distributed to the target tissues, metabolized effectively and excreted without causing adverse effects (Ononamadu *et al*., 2021). The PASS analysis further corroborates the potential of Duartin as a therapeutic agent by predicting a range of biological activities. PASS analysis employs a robust algorithm to envisage the activity (biological) spectrum of a compound and the results for Duartin indicate its

Table 2: ADME and Tox characteristics for Duartin are predicted *in silico*.

	Properties												
	Absorption	**Distribution**			**Metabolism**							**Excretion**	**Toxicity**
Models	Intestinal absorption (human)	VDss (human)	BBB permeability	CNS permeability	CYP							Total clearance	AMES toxicity/ Hepatoxicity
					Substrate		**Inhibitor**						
					2D6	3A4	1A2	2C19	2C9	2D6	3A4		
Unity	Numeric (% absorbed)	Numeric (log L/ kg)	Numeric (Log BB)	Numeric (Log PS)	Categorical (yes/no)							Numeric (log mL/ min / kg)	Categorical (yes/no)
Predicted values													
Duartin	91.013	0.059	-0.525	-2.987	NO	Yes	Yes	Yes	Yes	No	Yes	0.084	No/No

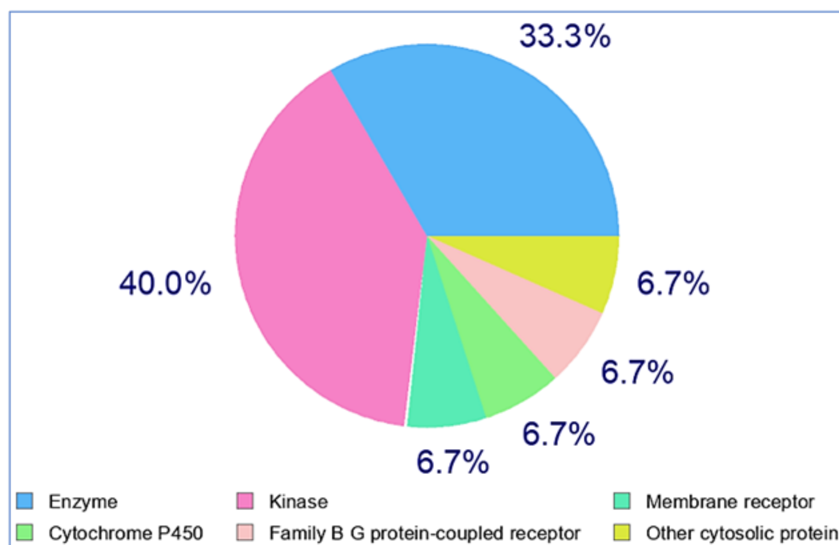


Figure 2: SwissTargetPrediction analysis showing diverse biological properties linked to Duartin.

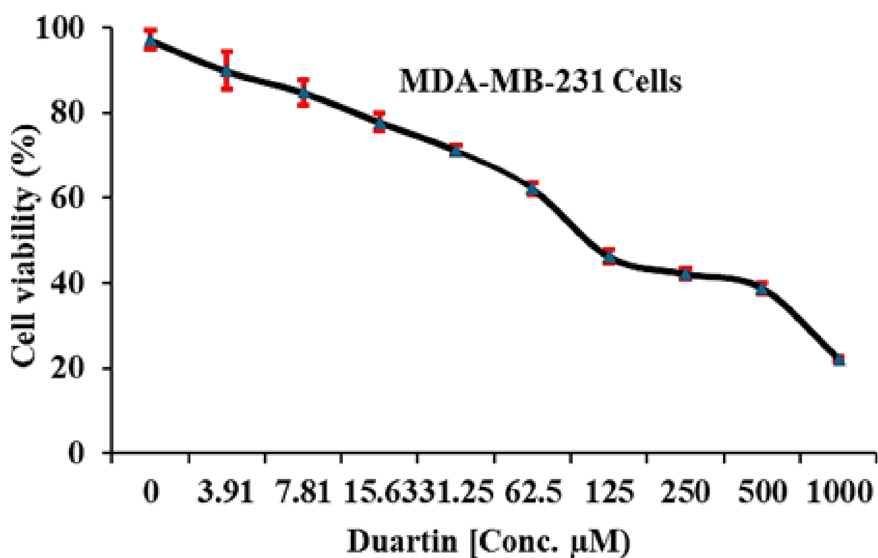
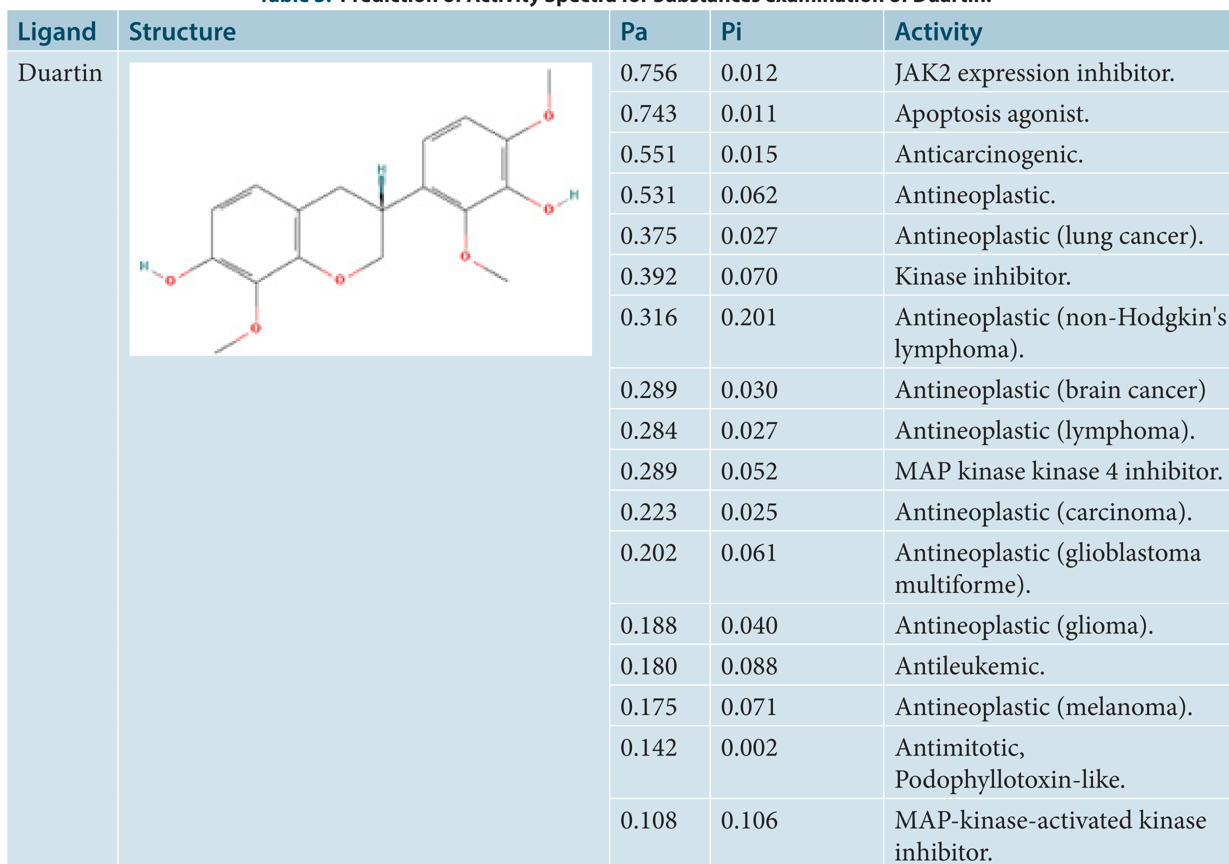


Figure 3: Concentration dependent cell toxicity effect of Duartin on breast cancer cells (MDA-MB-231).

Table 3: Prediction of Activity Spectra for Substances examination of Duartin.

Ligand	Structure	Pa	Pi	Activity
Duartin		0.756	0.012	JAK2 expression inhibitor.
		0.743	0.011	Apoptosis agonist.
		0.551	0.015	Anticarcinogenic.
		0.531	0.062	Antineoplastic.
		0.375	0.027	Antineoplastic (lung cancer).
		0.392	0.070	Kinase inhibitor.
		0.316	0.201	Antineoplastic (non-Hodgkin's lymphoma).
		0.289	0.030	Antineoplastic (brain cancer)
		0.284	0.027	Antineoplastic (lymphoma).
		0.289	0.052	MAP kinase kinase 4 inhibitor.
		0.223	0.025	Antineoplastic (carcinoma).
		0.202	0.061	Antineoplastic (glioblastoma multiforme).
		0.188	0.040	Antineoplastic (glioma).
		0.180	0.088	Antileukemic.
		0.175	0.071	Antineoplastic (melanoma).
		0.142	0.002	Antimitotic, Podophyllotoxin-like.
		0.108	0.106	MAP-kinase-activated kinase inhibitor.

Pa-Probability "to be active"; Pi-Probability "to be inactive".

potential efficacy in various pharmacological domains (Poroikov *et al*., 2000). This predictive capability is essential for early-stage drug discovery, as it helps in identifying promising candidates for further investigation. SwissTargetPrediction analysis supports the findings of the PASS analysis by providing insights into the potential molecular targets of Duartin (Daina *et al*., 2019). Together; these computational predictions affirm the drug-like properties of Duartin and highlights its potential as a good therapeutic agent, targeting Aurora A protein kinase in breast cancer. The convergence of favourable ADMET characteristics, a broad spectrum of predicted biological activities and multiple potential molecular targets positions Duartin as a promising candidate for further preclinical and clinical studies.

The concentration-dependent cell toxicity assay revealed that Duartin exerts a pronounced effect on the viability of breast cancer cells. Duartin, 13.42 μM, indicates that Duartin has a potent cytotoxic effect on these cells. This finding is crucial as it proposes that Duartin could potentially be developed as a therapeutic agent for breast cancer, specifically targeting MDA-MB-231 cells, which are known for their aggressive behaviour and resistance to certain treatments. Furthermore, the time-dependent cell toxicity assay provided additional insights into the cytotoxic dynamics of Duartin. The outcomes presented that prolonged exposure of MDA-MB-231 cells to the Duartin significantly reduced cell viability over a 48 hr period. This time-dependent decrease in viability highlights the sustained action of Duartin, suggesting that continuous exposure could be necessary for achieving optimal therapeutic effects. The significant reduction in cell viability with both concentration and time indicates that Duartin acts effectively at low micromolar concentrations and continues to impact cell survival over extended periods (Hashemnia *et al*., 2016; Pancholi *et al*., 2022). These findings are promising for the possible expansion of Duartin as a therapeutic agent.

Further, the results of this study also highlight the critical influence of Duartin on the regulation of Aurora A protein kinase mRNA expression in breast cancer cells (MDA-MB-231). The marked decrease in Aurora A mRNA levels following treatment with Duartin, suggests a potent inhibitory effect of Duartin. This finding is particularly significant with the well-established role of Aurora A kinase in the regulation of mitotic entry and progression, as well as its association with poor prognosis in various cancers, including breast cancer (Du *et al*., 2021; Nikhil and Shah, 2024). Furthermore, the impact of Duartin on Aurora A protein kinase mRNA expression may provide insights into its broader antitumor mechanisms. Aurora A kinase is a key player in the regulation of mitosis and its overexpression has been linked to chromosomal instability and tumorigenesis (Katayama *et al*., 2023). By significantly reducing the expression of this kinase, Duartin may help to restore normal cell cycle control and reduce the propagation of cancer cells.

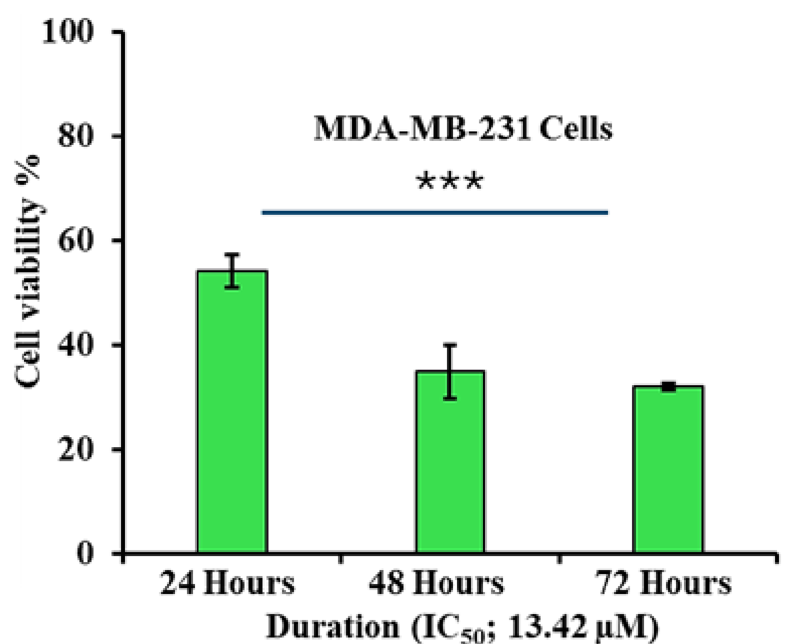


Figure 4: Time dependent cytotoxic effect of Duartin on breast cancer cells.

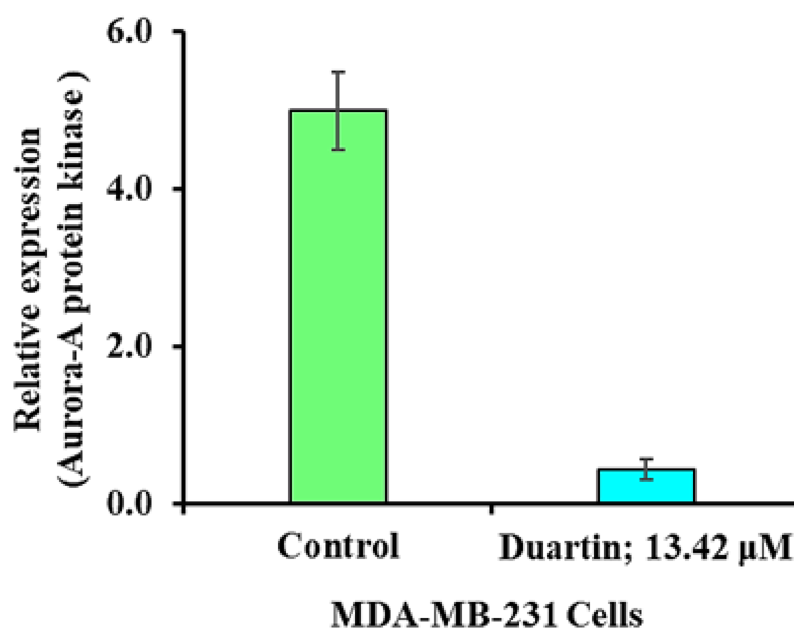


Figure 5: Effect of IC_{50} dose of Duartin on the mRNA expression of Aurora A protein kinase.

CONCLUSION

The study aimed to examine the binding affinity of various compounds with Aurora A protein kinase, a crucial enzyme in cell cycle regulation. Duartin exhibited the highest binding affinity, forming stable interactions with Aurora A protein kinase. ADMET properties, PASS and SwissTargetPrediction analyses affirm its drug-like properties. Duartin significantly reduced cell viability in breast cancer cells, portentous it's probable as a effective therapeutic agent. Its ability to decrease Aurora A mRNA levels indicates a strong inhibitory effect, potentially restoring normal cell cycle control and reducing cancer cell proliferation. Overall, the findings from this study indicate that the Duartin may emerge as a good therapeutic agent for further preclinical and clinical studies targeting breast cancer.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

ABBREVIATIONS

PDB: Protein Data Bank; **ADMET:** Absorption, Distribution, Metabolism, Excretion and Toxicity; **DMSO:** Dimethyl sulfoxide; **PASS:** Prediction of Activity Spectra for Substances.

SUMMARY

The study initiates that Duartin, a compound through the peak binding affinity to Aurora A protein kinase, has probable as a compelling therapeutic agent. It suggestively reduced cell viability in breast cancer cells, restoring normal cell cycle control and reducing cancer cell proliferation.

REFERENCES

Bhullar, K. S., Lagarón, N. O., McGowan, E. M., Parmar, I., Jha, A., Hubbard, B. P., & Rupasinghe, H. P. V. (2018). Kinase-targeted cancer therapies: Progress, challenges and future directions. Molecular Cancer, 17(1), 48. https://doi.org/10.1186/s12943-018-0804-2, PubMed: 29455673

Carmena, M., Ruchaud, S., & Earnshaw, W. C. (2009). Making the Auroras glow: Regulation of Aurora A and B kinase function by interacting proteins. Current Opinion in Cell Biology, 21(6), 796–805. https://doi.org/10.1016/j.ceb.2009.09.008, PubMed: 19836940

Chen, D., Oezguen, N., Urvil, P., Ferguson, C., Dann, S. M., & Savidge, T. C. (2016). Regulation of protein-ligand binding affinity by hydrogen bond pairing. Science Advances, 2(3), Article e1501240. https://doi.org/10.1126/sciadv.1501240, PubMed: 27051863

Daina, A., Michielin, O., & Zoete, V. (2019). SwissTargetPrediction: Updated data and new features for efficient prediction of protein targets of small molecules. Nucleic Acids Research, 47(W1), W357–W364. doi:0.1093/nar/gkz382. https://doi.org/10.1093/nar/gkz382, PubMed: 31106366

Du, R., Huang, C., Liu, K., Li, X., & Dong, Z. (2021). Targeting AURKA in Cancer: Molecular mechanisms and opportunities for Cancer therapy. Molecular Cancer, 20(1), 15. https://doi.org/10.1186/s12943-020-01305-3, PubMed: 33451333

Fu, J., Bian, M., Jiang, Q., & Zhang, C. (2007). Roles of Aurora kinases in mitosis and tumorigenesis. Molecular Cancer Research: MCR, 5(1), 1–10. https://doi.org/10.1158/1541-7786.MCR-06-0208, PubMed: 17259342

Goldenson, B., & Crispino, J. D. (2015). The aurora kinases in cell cycle and leukemia. Oncogene, 34(5), 537–545. https://doi.org/10.1038/onc.2014.14, PubMed: 24632603

Hashemnia, S. M. R., Atari-Hajipirloo, S., Roshan-Milani, S., Valizadeh, N., Mahabadi, S., & Kheradmand, F. (2016). Imatinib alters cell viability but not growth factors levels in TM4 Sertoli cells. International Journal of Reproductive Biomedicine, 14(9), 577–582. https://doi.org/10.29252/ijrm.14.9.577, PubMed: 27738659

Ingebriktsen, L. M., Humlevik, R. O. C., Svanøe, A. A., Sæle, A. K. M., Winge, I., Toska, K., Kalvenes, M. B., Davidsen, B., Heie, A., Knutsvik, G., Askeland, C., Stefansson, I. M., Hoivik, E. A., Akslen, L. A., & Wik, E. (2024). Elevated expression of Aurora-A/AURKA in breast cancer associates with younger age and aggressive features. Breast Cancer Research: BCR, 26(1), 126. https://doi.org/10.1186/s13058-024-01882-x, PubMed: 39198859

Jeng, Y.-M., Peng, S.-Y., Lin, C.-Y., & Hsu, H.-C. (2004). Overexpression and amplification of Aurora-A in hepatocellular carcinoma. Clinical Cancer Research: An Official Journal of the American Association for Cancer Research, 10(6), 2065–2071. https://doi.org/10.1158/1078-0432.ccr-1057-03, PubMed: 15041727

Katayama, H., Brinkley, W. R., & Sen, S. (2003). The Aurora kinases: Role in cell transformation and tumorigenesis. Cancer Metastasis Reviews, 22(4), 451–464. https://doi.org/10.1023/a:1023789416385, PubMed: 12884918

Katayama, H., Wang, J., Treekitkarnmongkol, W., Kawai, H., Sasai, K., Zhang, H., Wang, H., Adams, H. P., Jiang, S., Chakraborty, S. N., Suzuki, F., Arlinghaus, R. B., Liu, J., Mobley, J. A., Grizzle, W. E., Wang, H., & Sen, S. (2012). Aurora kinase-A inactivates DNA damage-induced apoptosis and spindle assembly checkpoint response functions of p73. Cancer Cell, 21(2), 196–211. https://doi.org/10.1016/j.ccr.2011.12.025, PubMed: 22340593

Keen, N., & Taylor, S. (2004). Aurora-kinase inhibitors as anticancer agents. Nature Reviews. Cancer, 4(12), 927–936. https://doi.org/10.1038/nrc1502, PubMed: 15573114

Kitzen, J. J., de Jonge, M. J., & Verweij, J. (2010). Aurora kinase inhibitors. Critical Reviews in Oncology/Hematology, 73(2), 99–110. https://doi.org/10.1016/j.critrevonc.2009.03.009, PubMed: 19369091

Lin, X., Xiang, X., Hao, L., Wang, T., Lai, Y., Abudoureyimu, M., Zhou, H., Feng, B., Chu, X., & Wang, R. (2020). The role of Aurora-A in human cancers and future therapeutics. American Journal of Cancer Research, 10(9), 2705–2729. PubMed: 33042612

Liu, B., Zhou, H., Tan, L., Siu, K. T. H., & Guan, X.-Y. (2024). Exploring treatment options in cancer: Tumor treatment strategies. Signal Transduction and Targeted Therapy, 9(1), 175. https://doi.org/10.1038/s41392-024-01856-7, PubMed: 39013849

Magnaghi-Jaulin, L., Eot-Houllier, G., Gallaud, E., & Giet, R. (2019). Aurora A protein kinase: To the centrosome and beyond. Biomolecules, 9(1), 28. https://doi.org/10.3390/biom9010028, PubMed: 30650622

Mehra, R., Serebriiskii, I. G., Burtness, B., Astsaturov, I., & Golemis, E. A. (2013). Aurora kinases in head and neck cancer. The Lancet. Oncology, 14(10), e425–e435. https://doi.org/10.1016/S1470-2045(13)70128-1, PubMed: 23993387

Nikhil, K., & Shah, K. (2024). The significant others of aurora kinase a in cancer: Combination is the key. Biomarker Research, 12(1), 109. https://doi.org/10.1186/s40364-024-00651-4, PubMed: 39334449

Nowakowski, J., Cronin, C. N., McRee, D. E., Knuth, M. W., Nelson, C. G., Pavletich, N. P., Rogers, J., Sang, B.-C., Scheibe, D. N., Swanson, R. V., & Thompson, D. A. (2002). Structures of the cancer-related Aurora-A, FAK and EphA2 protein kinases from nanovolume crystallography. Structure, 10(12), 1659–1667. https://doi.org/10.1016/s0969-2126(02)00907-3, PubMed: 12467573

Ononamadu, C. J., & Ibrahim, A. (2021). Molecular docking and prediction of ADME/drug-likeness properties of potentially active antidiabetic compounds isolated from aqueous-methanol extracts of Gymnema sylvestre and Combretum micranthum. Biotechnologia, 102(1), 85–99. https://doi.org/10.5114/bta.2021.103765, PubMed: 36605715

Pancholi, S., Simigdala, N., Ribas, R., Schuster, E., Leal, M. F., Nikitorowicz-Buniak, J., Rega, C., Bihani, T., Patel, H., Johnston, S. R., Dowsett, M., & Martin, L.-A. (2022). Elacestrant demonstrates strong anti-estrogenic activity in PDX models of estrogen-receptor positive endocrine-resistant and fulvestrant-resistant breast cancer. npj Breast Cancer, 8(1), 125. https://doi.org/10.1038/s41523-022-00483-1, PubMed: 36446866

Panigrahi, S. K., & Desiraju, G. R. (2007). Strong and weak hydrogen bonds in the protein-ligand interface. Proteins, 67(1), 128–141. https://doi.org/10.1002/prot.21253, PubMed: 17206656

Pitsawong, W., Buosi, V., Otten, R., Agafonov, R. V., Zorba, A., Kern, N., Kutter, S., Kern, G., Pádua, R. A., Meniche, X., & Kern, D. (2018). Dynamics of human protein kinase Aurora A linked to drug selectivity. eLife, 7, Article e36656. https://doi.org/10.7554/eLife.36656, PubMed: 29901437

Poroikov, V. V., Filimonov, D. A., Borodina, Y. V., Lagunin, A. A., & Kos, A. (2000). Robustness of biological activity spectra predicting by computer program PASS for noncongeneric sets of chemical compounds. Journal of Chemical Information and Computer Sciences, 40(6), 1349–1355. https://doi.org/10.1021/ci000383k

Roshan, P., Kuppa, S., Mattice, J. R., Kaushik, V., Chadda, R., Pokhrel, N., Tumala, B. R., Biswas, A., Bothner, B., Antony, E., & Origanti, S. (2023). An Aurora B-RPA signaling axis secures chromosome segregation fidelity. Nature Communications, 14(1), 3008. https://doi.org/10.1038/s41467-023-38711-2, PubMed: 37230964

Sasai, K., Parant, J. M., Brandt, M. E., Carter, J., Adams, H. P., Stass, S. A., Killary, A. M., Katayama, H., & Sen, S. (2008). Targeted disruption of Aurora A causes abnormal mitotic spindle assembly, chromosome misalignment and embryonic lethality. Oncogene, 2998, 27(29), 4122–4127. https://doi.org/10.1038/onc.2008.47, PubMed: 18345035

Sen, S., Zhou, H., & White, R. A. (1997). A putative serine/threonine kinase encoding gene BTAK on chromosome 20q13 is amplified and overexpressed in human breast cancer cell lines. Oncogene, 14(18), 2195–2200. https://doi.org/10.1038/sj.onc.1201065, PubMed: 9174055

Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians, 71(3), 209–249. https://doi.org/10.3322/caac.21660, PubMed: 33538338

Takeshita, M., Koga, T., Takayama, K., Ijichi, K., Yano, T., Maehara, Y., Nakanishi, Y., & Sueishi, K. (2013). Aurora-B overexpression is correlated with aneuploidy and poor prognosis in non-small cell lung cancer. Lung Cancer, 80(1), 85–90. https://doi.org/10.1016/j.lungcan.2012.12.018, PubMed: 23313006

Torchia, E. C., Chen, Y., Sheng, H., Katayama, H., Fitzpatrick, J., Brinkley, W. R., Caulin, C., Sen, S., & Roop, D. R. (2009). A genetic variant of Aurora kinase A promotes genomic instability leading to highly malignant skin tumors. Cancer Research, 69(18), 7207–7215. https://doi.org/10.1158/0008-5472.CAN-09-1059, PubMed: 19738056

Trott, O., & Olson, A. J. (2010). AutoDock Vina: Improving the speed and accuracy of docking with a new scoring function, efficient optimization and multithreading. Journal of Computational Chemistry, 31(2), 455–461. https://doi.org/10.1002/jcc.21334, PubMed: 19499576

Wang, P., Gong, Y., Guo, T., Li, M., Fang, L., Yin, S., Kamran, M., Liu, Y., Xu, J., Xu, L., Peng, F., Xue, X., Yang, M., Hung, M.-C., Lam, E. W.-F., Gu, C., Wang, C., Zhan, Q., & Liu, Q. (2019). Activation of aurora A kinase increases YAP stability via blockage of autophagy. Cell Death and Disease, 10(6), 432. https://doi.org/10.1038/s41419-019-1664-4, PubMed: 31160567

Wang, X. X., Liu, R., Jin, S. Q., Fan, F. Y., & Zhan, Q. M. (2006). Overexpression of Aurora-A kinase promotes tumor cell proliferation and inhibits apoptosis in esophageal squamous cell carcinoma cell line. Cell Research, 16(4), 356–366. https://doi.org/10.1038/sj.cr.7310046, PubMed: 16617331

Willems, E., Dedobbeleer, M., Digregorio, M., Lombard, A., Lumapat, P. N., & Rogister, B. (2018). The functional diversity of Aurora kinases: A comprehensive review. Cell Division, 13, 7. https://doi.org/10.1186/s13008-018-0040-6, PubMed: 30250494

Zhang, J., Ma, J., Li, Y., An, Y., Du, W., Yang, Q., Huang, M., & Cai, X. (2024). Overexpression of Aurora kinase B is correlated with diagnosis and poor prognosis in hepatocellular carcinoma. International Journal of Molecular Sciences, 25(4), 2199. https://doi.org/10.3390/ijms25042199, PubMed: 38396874

Zhang, Y., Ma, Y., Wang, Y., Mukhopadhyay, D., Bi, Y., & Ji, B. (2022). Aurora kinase a inhibitor MLN8237 suppresses pancreatic cancer growth. Pancreatology, 22(5), 619–625. https://doi.org/10.1016/j.pan.2022.03.019, PubMed: 35550115

Zheng, D., Li, J., Yan, H., Zhang, G., Li, W., Chu, E., & Wei, N. (2023). Emerging roles of Aurora-A kinase in cancer therapy resistance. Acta Pharmaceutica Sinica. B, 13(7), 2826–2843. https://doi.org/10.1016/j.apsb.2023.03.013, PubMed: 37521867

Zorba, A., Buosi, V., Kutter, S., Kern, N., Pontiggia, F., Cho, Y.-J., & Kern, D. (2014). Molecular mechanism of aurora A kinase autophosphorylation and its allosteric activation by TPX2. eLife, 3, Article e02667. https://doi.org/10.7554/eLife.02667, PubMed: 24867643

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