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Original Article

Evaluating Myricetin as a CDK2 Inhibitor in Lung Cancer: *In silico* and *in vitro* Assessment of a Flavonoid-Based Small Molecule

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ABSTRACT

Background: Inhibiting Cyclin-Dependent Kinase 2 (CDK2) holds significant therapeutic potential for lung cancer by targeting a critical regulator of the cell cycle. CDK2 inhibition halts cancer cell proliferation, induces apoptosis, and disrupts tumor progression. Flavonoids have recognized to be exceedingly effective in treating a wide range of diseases, together with cardiovascular, immunological disorders, and cancer. **Materials and Methods:** This study intended to investigate the possible of flavonoid small molecules as CDK2 inhibitors. We examined the potential of the lead compound, myricetin, as a CDK2 inhibitor and its cytotoxic effects on A549 lung carcinoma cells using *in silico* and *in vitro* methods. **Results:** Molecular docking revealed a high binding affinity, -8.6 kcal/mol, of myricetin to CDK2, with interactions involving key amino acid residues, including hydrogen bonds with ASP86, ASP145, and ASN132, as well as various other non-covalent interactions. ADMET analysis demonstrated favourable pharmacokinetic properties of myricetin, with promising predictions for kinase inhibition, apoptosis induction, and anticancer activity. Swiss Target Prediction highlighted myricetin's potential to modulate diverse biological targets, including enzymes, kinases, and G-protein-coupled receptors. Myricetin exhibited a concentration- and time-dependent cytotoxic effect on A549 cells, with an IC_{50} of 93.41 µM. Cell viability decreased significantly up to 48 hr but then plateaued. Myricetin also significantly downregulated CDK2 mRNA expression and activity in a dose-dependent manner, with reductions observed across half, IC_{50}, and double IC_{50} concentrations. **Conclusion:** These findings suggest that myricetin is a promising candidate for CDK2 inhibition and lung cancer treatment, warranting further investigation into its mechanism of action and therapeutic potential.

Keywords: CDK2 inhibition, Flavonoids, Lung cancer, Molecular docking, Myricetin.

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INTRODUCTION

Lung cancer remains one of the record prevalent and deadly cancers worldwide, with non-small cell lung cancer accounting for approximately 85% of cases.[1-3] Despite advancements in targeted therapies and immunotherapies, the prognosis for many lung cancer patients remains poor, particularly for those with advanced or metastatic disease.[4,5] Traditional treatments, including surgery, chemotherapy, and radiation therapy, often have partial efficacy and are connected with important side effects.[6,7] Consequently, there is an unmet necessity for the progress of novel, more effective therapeutic molecules and strategies.

CDKs (Cyclin-Dependent Kinases) are a family of serine/threonine protein kinases that show a key role in cell cycle regulation and transcription.[8-10] Dysregulation of CDKs, particularly CDK2, has been implicated in various cancers, including lung cancer.[10,11] CDK2 is primarily tangled in the transition from the G1 to the S phase of the cell cycle through its interaction with cyclins E and A.[10,12,13] This regulation ensures accurate DNA replication and cell proliferation. Aberrant CDK2 activity, often resulting from overexpression of cyclins or loss of regulatory checkpoints, leads to uncontrolled cellular proliferation, a hallmark of cancer.[10]

CDK2 overactivation has been associated with tumour progression, resistance to therapy, and poor prognosis in lung cancer.[14-18] Unlike other CDKs such as CDK4/6, which have FDA-approved inhibitors (e.g., palbociclib, ribociclib), CDK2 lacks specific clinical inhibitors. However, recent studies suggest that selective inhibition of CDK2 can impair cancer cell proliferation and induce apoptosis, particularly in tumours that rely on CDK2-driven pathways.[19,20] For instance, CDK2 activity is

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critical in cancers with amplification of cyclin E or loss of p27, a key CDK2 inhibitor.[21,22]

The therapeutic potential of CDK2 inhibition lies in its ability to specifically target cancer cells while sparing normal cells. This specificity arises from the dependency of certain cancers on CDK2 for survival, a phenomenon termed "oncogene addiction".[23] In lung cancer, targeting CDK2 may also enhance the efficacy of existing treatments, such as chemotherapies or immunotherapies, by overcoming resistance mechanisms.[16]

In silico methods, encompassing computational modelling, molecular docking, virtual screening, and molecular dynamics simulations, have developed drug discovery through allowing the identification and optimization of potential therapeutic agents with high precision and efficiency.[24,25] These methods reduce the time and cost associated with experimental drug development while providing valuable insights into molecular interactions and binding mechanism.[26,27]

Naturally occurring flavonoid small molecules have garnered significant attention for their therapeutic potential in treating a variety of diseases, including cardiovascular diseases, neuronal disorders, inflammation, and cancer.[28-33] Their broad pharmacological properties, as well as antioxidant, anti-inflammatory, and anticancer activities, make them promising candidates for therapeutic development.[31-33] Flavonoids can modulate key molecular pathways involved in disease progression, such as reducing oxidative stress, inhibiting pro-inflammatory cytokines, and enhancing cellular apoptosis in cancer cells.[34-36] Their ability to target multiple disease mechanisms positions them as versatile therapeutic agents.

This present study was aimed to investigate the potential of flavonoid small molecules as CDK2 inhibitors. We examined the potential of the lead compound, myricetin, as a CDK2 inhibitor and its cytotoxic effects on A549 lung carcinoma cells using *in silico* and *in vitro* methods. The integration of computational and experimental methods will ensure the development of robust, clinically translatable inhibitors, contributing to improved outcomes for lung cancer patients.

MATERIALS AND METHODS

Preparation of CDK2 structure

The high resolution (1.90 Å) crystal structure of human CDK2 (Cyclin-Dependent Kinase 2) (PDB ID: 1HCK) was downloaded from RCSB PDB database.[37] The structure was prepared by eliminating water molecules, bound ligands, and heteroatoms unless necessary for docking.[38,39] Next, hydrogen atoms were assigned to the protein, ensuring correct protonation states at physiological pH.[40] This was done using the Auto Dock Tools. Swiss-PDB Viewer tools were used to check and correct any structural issues in the protein molecule, such as missing atoms, unseemly bond orders, or unresolved residues. Further, energy minimization was performed to repair distorted geometries by moving atoms and releasing internal constraints on the protein structure. Finally, charges such as Hydrogen atoms and Kollman United Atom Charges were added to the protein structure, ensuring accurate electrostatic interactions during docking. The structure was kept in. pdbqt format, a suitable format for molecular docking using Auto Dock Tools.

Preparation of small library of flavonoid small molecules

Twenty-seven plant-derived flavonoid small molecules were selected for screening against a target protein. Flavonoids have demonstrated great effectiveness in treating a wide variety of diseases, from cardiovascular and immunological disorders to cancer.[32,41] The structures of these ligand molecules were downloaded in mol format from the PubChem (https://pubchem.ncbi.nlm.nih.gov/) 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 modelling software. Appropriate atomic charges were subsequently assigned to the ligand molecules. Finally, the optimized and corrected ligand structures were converted into docking-compatible. pdbqt format using MGL Tools.

Molecular docking of flavonoid small molecules with CDK2

AutoDock Vina was used for the molecular docking of flavonoid small molecules with CDK2. The grid dimensions for the X, Y, and Z coordinates were set to 49, 51, and 59 Å, respectively, cantered at -36.33, 14.14, and 55.23. 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 using PyMOL and Discovery Studio Visualizer to determine the interaction patterns between the flavonoid small molecules and the CDK2.

ADMET properties of myricetin

The ADMET properties of predicted lead molecule "myricetin" were determined via Swiss ADME (http://www.swissadme.ch/index.php) & pkCSM

(https://biosig.lab.uq.edu.au/pkcsm/). SMILES strings of myricetin were integrated to web-based platforms of these tools to expect the ADMET properties of myricetin.

Prediction of Biological Activity Spectrum of myricetin

The web-based flatforms namely PASS (Prediction of Activity Spectra for Substances) Online (http://www.pharmaexpert.ru/passonline/) & the Swiss Target Prediction (http://www.swisstargetprediction.ch/) were used to ascertain the Biological Activity Spectrum and pharmacological activities connected with the ligand molecule "myricetin". SMILES strings of myricetin were integrated to web-based platforms of PASS Online and Swiss Target Prediction tools.

Viability assay

A549 lung carcinoma cells were seeded into a 96-well plate at the desired density (e.g., 5,000-10,000 cells/well). Plate was incubated at 37°C in a CO_2 incubator for the period of 24 hr to allow cell attachment. Exhausted media was replaced with fresh culture media containing the desired concentrations (0-2000 µM) of test compound, myricetin. Plates were incubated for 72 hr. MTT stock solution (typically 5 mg/mL in PBS) was prepared and extra to each well (usually 10-20 µL of stock per 100 µL medium). Plates were incubated at 37°C for 2-4 hr. During this time, mitochondrial enzymes in viable cells will reduce MTT to formazan crystals. The supernatant was removed carefully without disturbing the crystals. DMSO (100-200 µL) was added to each well and placed the plate on a shaker to dissolve the formazan crystals. Absorbance was recorded at 570 nm using a microplate reader. Average absorbance was calculated for each condition and the results were expressed as a percentage of viable cells related to the untreated control: Cell viability (%) = (Sample absorbance/Control absorbance) ×100. Results were plotted as a dose-response curve, testing multiple concentrations. The IC_{50} concentration of myricetin was calculated. Additionally, a time-dependent cell viability assay was executed at 12, 24, 36, 48, 60, and 72 hr in cells treated by IC_{50} concentration of myricetin.

mRNA expression

A549 lung carcinoma cells were treated thru the IC_{50} concentration of myricetin for 24 hr. Cells were harvested under sterile conditions and RNA was extracted using RNA extraction kit (TRIzol Reagent) (Almanac). RNA concentration was measured using a spectrophotometer (Nano Drop) and RNA integrity was checked with gel electrophoresis. 1µg of total RNA was used for reverse transcription to synthesize the cDNA using cDNA synthesis kit (Almanac). qPCR reaction was prepared and run on a real-time PCR machine (Applied Biosystems). Ct (threshold cycle) values from the qPCR machine were analysed and relative mRNA expression was calculated using the $2^{-\Delta\Delta Ct}$ method. The primer sequences used for the amplification was as: CDK2-Forward: GAATCTCCAGGGAATAGGGC, CDK2-Reverse: CTGAAATCCTCCTGGGCTG, 18S-Forward: GGCCCTGTAATTGGAATGAGTC and 18S-Reverse: CCAAGATCCAACTACGAGCTT. Further, CDK2 activity in the extract of A549 lung carcinoma cells was quantified using the Human CDK2 ELISA (Enzyme-linked immunosorbent assay) Kit (Abcam; Cat#ab316258).

RESULTS

Binding energy

The binding affinities of top flavonoid small molecules are presented in Table 1. The peak binding affinity, -8.6 kcal/mol was detected between myricetin and the CDK2. Figure 1A-C represents the cartoon representation (1A), surface view representing binding of myricetin with in deep groove of CDK2 (1B), and 2D structure of docked complex showing interaction of myricetin with various amino acid residues of CDK2 (1C). Figure 1C shows that myricetin formed hydrogen bonds with the ASP86, ASP145, and ASN132 amino acid residues of CDK2. Myricetin also formed various other interactions, including van der Waals interactions with LYS129, GLY13, THR14, GLU12, GLN131, LYS89, GLN85, HIS84, LEU83, PHE82, ALA31, ALA144, and LYS33, Pi-Sigma bonds with ILE10 AND LEU134, and Pi-Alkyl bond with VAL18 amino acid residues of CDK2. These findings highlight myricetin's potential as a promising CDK2 inhibitor.

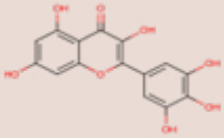
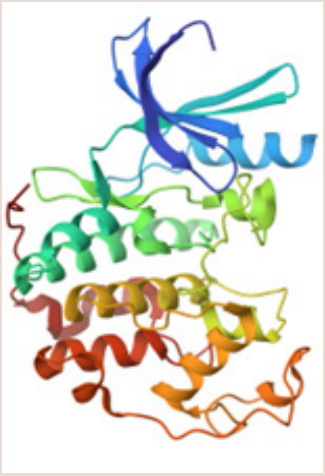
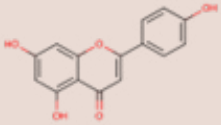
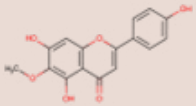
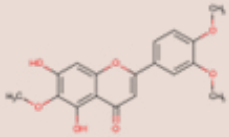
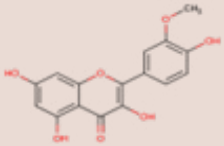
Prediction of biological activity spectrum and ADMET properties of myricetin

Results of the analysis of biological activity spectrum of myricetin are represented in Table 2 and Figure 2 respectively. These results demonstrated diverse biological properties associated with myricetin specific to cancer. Results of PASS analysis showed higher probability to kinase inhibition, apoptosis agonist, antineoplastic, anticarcinogenic, and JAK2 expression inhibitor (Table 2). Swiss Target Prediction analysis showed higher probability of myriceting to inhibit the diverse class of biological macromolecules such as Isomerase, Eraser, Unclassified proteins, Cytochrome P450, Primary active transporter, Hydrolase, Oxidoreductase, G protein-coupled receptor, Protease, Lyase, Enzyme, and Kinases (Figure 2). Results of the ADMET properties of myricetin are represented in Table 3, demonstrating favourable properties of myricetin in terms of absorption, distribution, metabolism, excretion, and toxicity.

Cytotoxic effect of myricetin on the viability of A549 lung carcinoma cells

Figures 3A & 3B and Figure 3C represents the concentration-dependent and time-dependent effect of myricetin on the viability of A549 lung carcinoma cells. Results of dose response curve showed statistically significant decrease ($p<0.001$) in the viability of cancer cells corresponding to increase in concentration of myricetin (Figure 3B). Significant decrease ($p<0.01$) in cell viability with respect to dese response curve was observed up to 48 hr. However, no significant decrease was observed in the cell viability from 48 to 72 hr.

Table 1: Binding affinities of top five small flavonoid ligand molecules with the target protein, CDK2.

Name of the ligand	Target protein	Binding Energy (kcal/mol)	*pKi*
Myricetin (DB02375) 	CDK2 	-8.6	3.41
Apigenin (DB07352) 		-5.1	2.22
Hispidulin (DB14008) 		-5.0	2.71
Eupatilin (DB16885) 		-4.5	2.40
Isorhamnetin (DB16767) 		-4.2	3.37

Further, IC_{50} concentration of myricetin was calculated to be 93.41 µM. Moreover, results of the time dependent effect of IC_{50} concentration of myricetin on the viability of lung carcinoma cells presented that there was a significant decrease ($p<0.01$) in viability of cells from 0 to 24 and 24 to 48 hr only. No significant decrease in viable cells was observed from 48 to 72 hr (Figure 3C).

CDK2 mRNA expression in myricetin treated A549 lung carcinoma cells

The expression (mRNA) levels of CDK2 in A549 lung carcinoma cells treated with half concentration of IC_{50} dose (46.705 µM), IC_{50} dose (93.41 µM), and double concentration of IC_{50} dose (186.82 µM) of myricetin are depicted in Figure 4A. Results showed that all the three concentrations significantly decreased ($p<0.01$ between control and IC_{50} dose group; $p<0.01$ between half concentration of IC_{50} dose and IC_{50} dose group; and $p<0.05$ between IC_{50} dose and double concentration of IC_{50} dose group) the expression of CDK2 in treated groups. These results also highlight the concentration dependent effect of myricetin on CDK2 expression.

CDK2 activity in myricetin treated A549 lung carcinoma cells

The activity levels of CDK2 in A549 lung carcinoma cells treated with half concentration of IC_{50} dose (46.705 µM), IC_{50} dose (93.41 µM), and double concentration of IC_{50} dose (186.82 µM) of myricetin are depicted in Figure 4B. Results showed that all the three concentrations significantly decreased ($p<0.001$ between control and IC_{50} dose group; $p<0.05$ between half concentration of IC_{50} dose and IC_{50} dose group; and $p<0.05$ between IC_{50} dose and double concentration of IC_{50} dose group) the CDK2 levels in treated groups. These results also highlight the concentration dependent effect of myricetin on CDK2 activity levels.

DISCUSSION

The current study demonstrates the possible of myricetin as a CDK2 inhibitor. Inhibiting CDK2 holds significant therapeutic potential for lung cancer by targeting a critical regulator of the cell cycle. CDK2 inhibition halts cancer cell proliferation, induces apoptosis, and disrupts tumor progression.[17,34,42] As a key driver in oncogenesis, CDK2 represents a promising target, offering a pathway for developing selective, effective anticancer

therapies.[19,20] The interaction profile between myricetin and CDK2 reveals a strong and specific binding mechanism. Myricetin formed hydrogen bonds with ASP86, ASP145, and ASN132 residues, which are critical for maintaining the structural integrity and functional activity of CDK2. The additional van der Waals interactions, Pi-Sigma bonds, and Pi-Alkyl bonds further stabilize the myricetin-CDK2 complex, highlighting a multidimensional interaction network. These outcomes are in alignment with earlier studies suggesting the importance of hydrogen bonding and hydrophobic interactions in kinase inhibition.[43-45] The molecular interactions reveal the ability of myricetin to target the active site of CDK2, emphasizing its potential to act as a competitive inhibitor. The involvement of amino acid residues such as LYS129, GLY13, and THR14, which are located near the ATP-binding pocket of CDK2, reinforces its capability to disrupt kinase activity.[46] These findings pave the way for further optimization of myricetin as selective CDK2 inhibitors for cancer therapy.

The ADMET analysis underscores myricetin's favourable pharmacokinetic properties, making it a promising candidate for drug development. Myricetin demonstrated suitable and acceptable toxicity ADMET properties profile. These characteristics indicate its potential for systemic administration with minimal adverse effects.[47,48] Further, the predicted biological activity spectrum of myricetin reveals its multifunctional nature. The high probability of kinase inhibition aligns with its molecular docking results and its inhibitory effects on CDK2. Furthermore, the prediction of myricetin as an apoptosis agonist, antineoplastic, and anticarcinogenic agent highlights its potential utility in cancer treatment. The ability to inhibit JAK2 expression and other key biological targets further emphasizes its versatility in modulating multiple pathways associated with cancer progression.[35,49] Swiss Target Prediction analysis indicated that myricetin interacts with a diverse range of biological macromolecules, including enzymes, kinases, and cytochrome P450 proteins. This broad spectrum of activity suggests that myricetin may exert pleiotropic effects in cellular systems, which could be helpful to develop combination

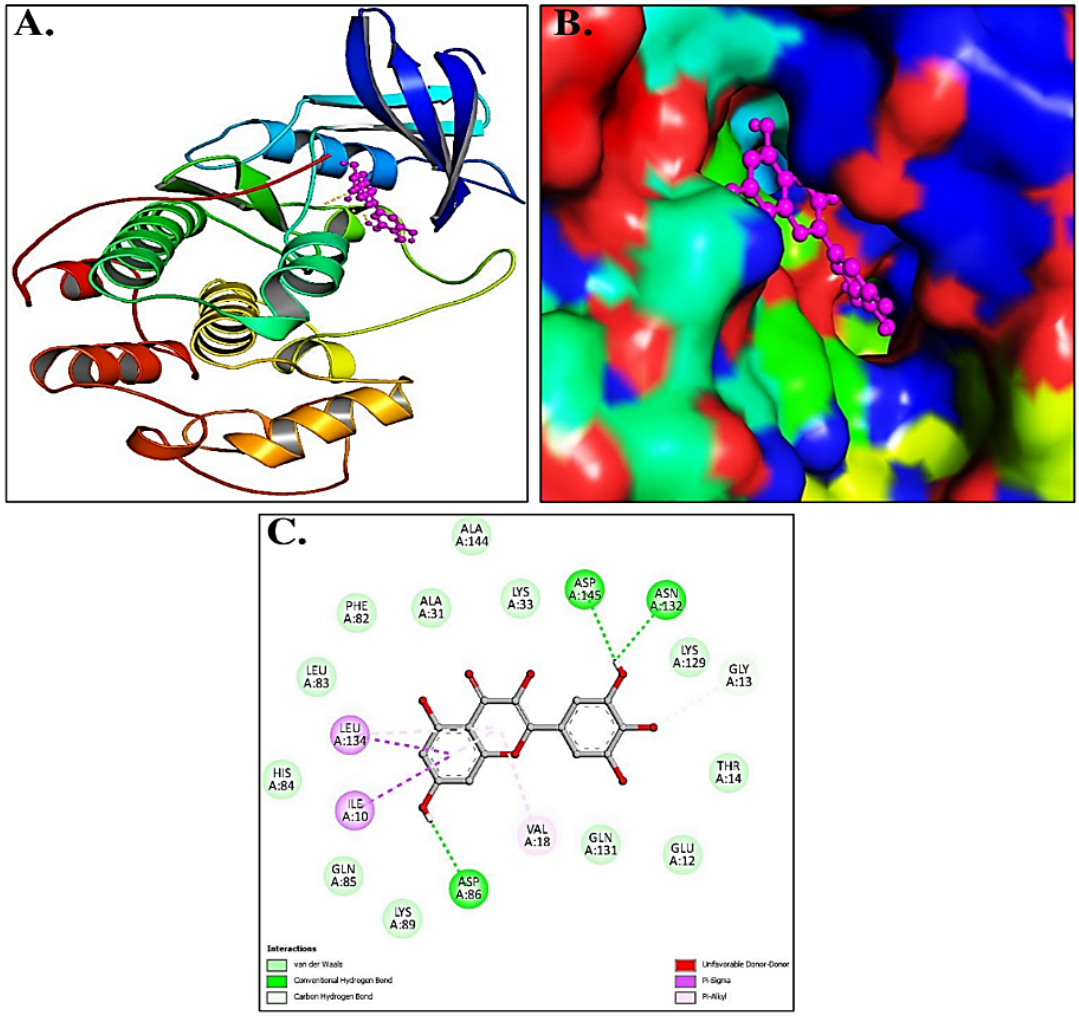
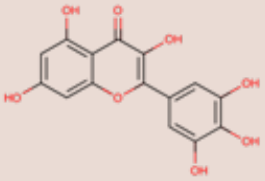


Figure 1: Molecular docking of myricetin with CDK2. (A) Cartoon representation, (B) Surface view representing binding of myricetin with in deep groove, and (C) 2D docked complex showing interaction of myricetin with various amino acid residues of CDK2.

Table 2: PASS study of Myricetin. Probability "to be active" was set at Pa>0,7.

Compound	Structure	Pa	Pi	Activity
Myricetin		0,958	0,001	Kinase inhibitor
		0,915	0,004	Apoptosis agonist
		0,841	0,008	Antineoplastic
		0,784	0,006	Anticarcinogenic
		0,733	0,014	JAK2 expression inhibitor

Pa - probability "to be active"); Pi - probability "to be inactive".

Table 3: ADME and Toxicity properties for Myricetin (MT).

Properties													
	Absorption	Distribution			Metabolism							Excretion	Toxicity
Models	Intestinal absorption (human)	VDss (human)	BBB permeability	CNS permeability	CYP							Total clearance	AMES/ Hepatotoxicity
					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													
MT	65.93	1.317	-1.413	-3.709	No	No	Yes	No	No	No	No	0.422	No/ No

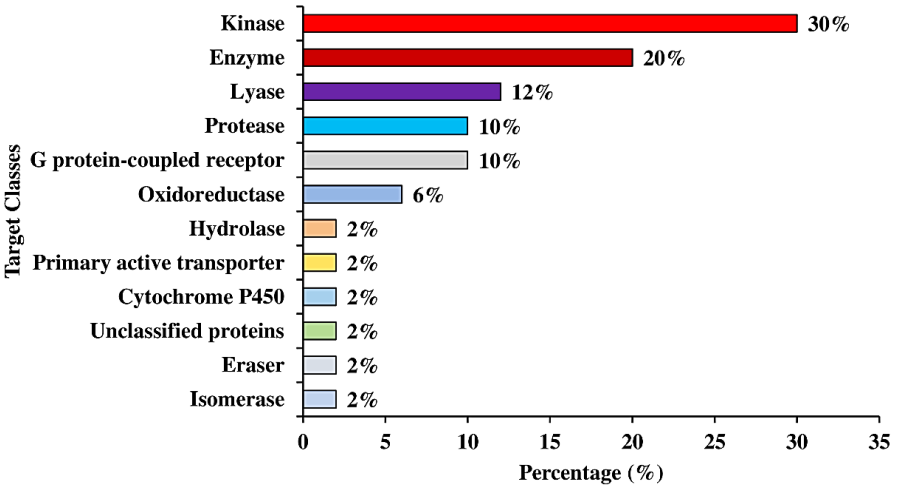


Figure 2: SwissTargetPrediction analysis showing diverse biological properties connected with myricetin.

therapies targeting multiple oncogenic pathways simultaneously. However, the interaction with cytochrome P450 enzymes warrants careful consideration, as it could influence drug metabolism and lead to potential drug-drug interactions.

The cytotoxic activity of myricetin against A549 lung carcinoma cells was found to be both concentration and time-dependent. The IC_{50} concentration of 93.41 µM demonstrated its potent anticancer effect. A statistically significant decrease in cell viability was observed with increasing concentrations of myricetin, particularly up to 48 hr. The lack of further reduction in cell viability beyond 48 hr may indicate the saturation of myricetin's cytotoxic effect or the activation of compensatory survival pathways in the cancer cells.[50] These findings suggest that myricetin effectively induces cytotoxicity in lung cancer cells within a specific concentration and time window, making it a auspicious candidate for more examination in preclinical and clinical studies. However, understanding the underlying mechanisms of cell death, whether it involves apoptosis, autophagy, or other pathways, is critical for optimizing its therapeutic application. Further the concentration-dependent downregulation of CDK2 mRNA expression upon treatment with myricetin provides persuasive evidence for its targeted action against CDK2. The significant reduction in mRNA levels across all tested concentrations

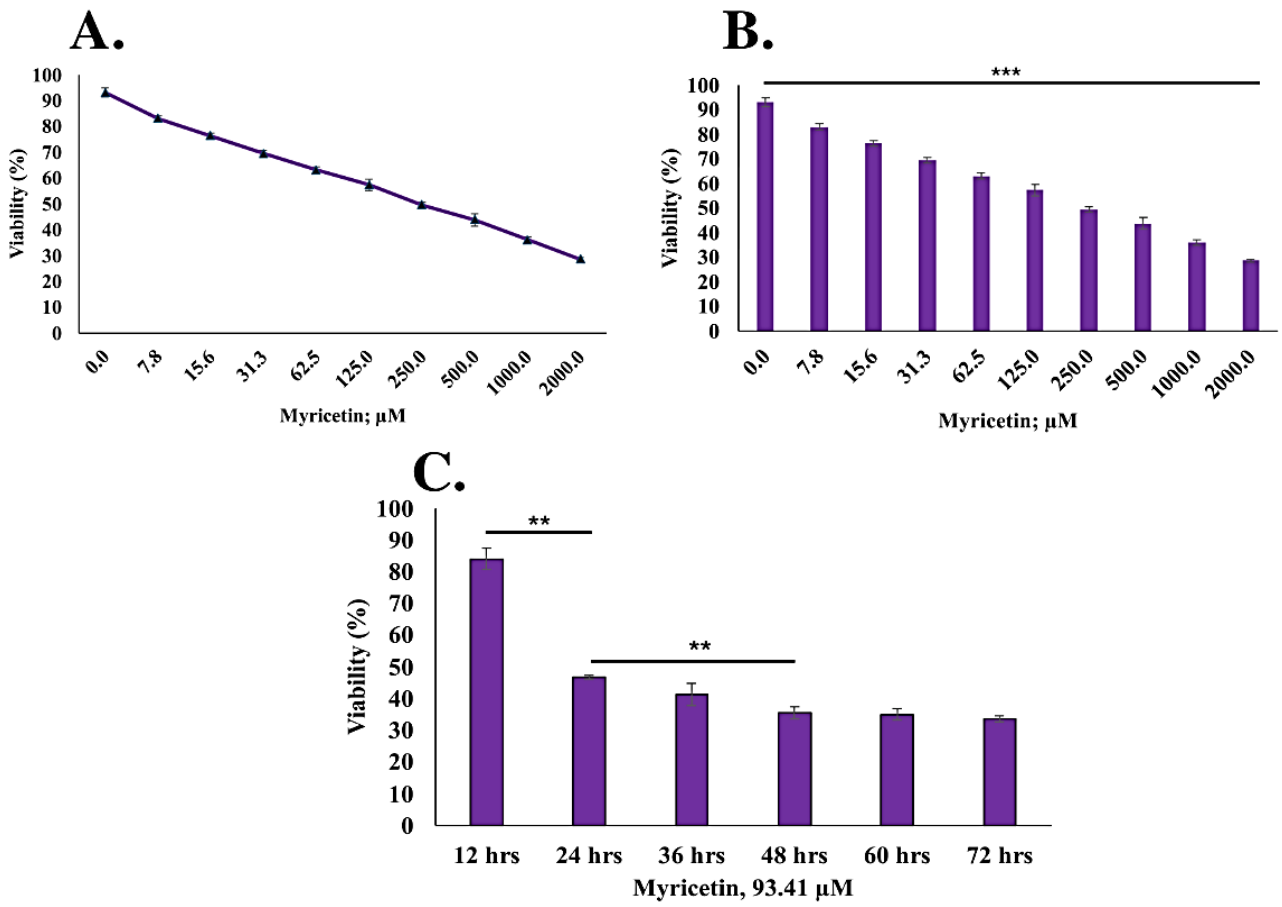


Figure 3: (A&B) Concentration dependent cell viability of myricetin treated A549 lung cancer cells. (C) Time dependent cell viability of myricetin treated A549 lung cancer cells.

highlights its effectiveness at both low and high doses. This effect was particularly found pronounced at the IC_{50} concentration (93.41 µM), highlighting its optimal activity at this dose. The observed decrease in CDK2 mRNA levels suggests that myricetin may interfere with transcriptional regulation or promote mRNA degradation. Such modulation of CDK2 expression is crucial, as CDK2 is a key regulator of the cell cycle and its overexpression is often associated with tumorigenesis.[51,52] By targeting CDK2 at the transcriptional level, myricetin could effectively halt cell cycle progression and impede cancer cell proliferation. In addition to its effects on mRNA expression, myricetin was shown to significantly reduce CDK2 activity in a concentration-dependent manner. This dual effect on both expression and activity levels highlights myricetin's comprehensive mechanism of action against CDK2. The significant decrease in CDK2 activity at the IC_{50} dose (93.41 µM) further validates its inhibitory potential. The reduction in CDK2 activity likely results from myricetin's ability to bind to its active site, as demonstrated by molecular docking studies. This inhibition disrupts the phosphorylation events necessary for cell cycle progression, principal to cell cycle arrest and subsequent apoptosis.[8] These findings align with the cytotoxic effects observed in A549 cells, providing a mechanistic explanation for myricetin's anticancer activity.

The collective results of this study highlight myricetin's potential as a novel therapeutic agent for lung cancer. Its ability to inhibit CDK2 through both transcriptional and enzymatic mechanisms highlights its targeted action against a key driver of cancer cell proliferation. Furthermore, the favourable ADMET properties and diverse biological activity spectrum of myricetin position it as a promising candidate for further development. The concentration- and time-dependent cytotoxic effects of myricetin on A549 cells suggest its potential for dose optimization in clinical settings. The observed saturation in cytotoxicity beyond 48 hr indicates that intermittent dosing schedules may be effective in maintaining therapeutic efficacy while minimizing potential toxicity. Additionally, the broad spectrum of targets identified through Swiss Target Prediction analysis suggests that myricetin could be used in combination therapies to target multiple pathways simultaneously, potentially overcoming resistance mechanisms in cancer cells.

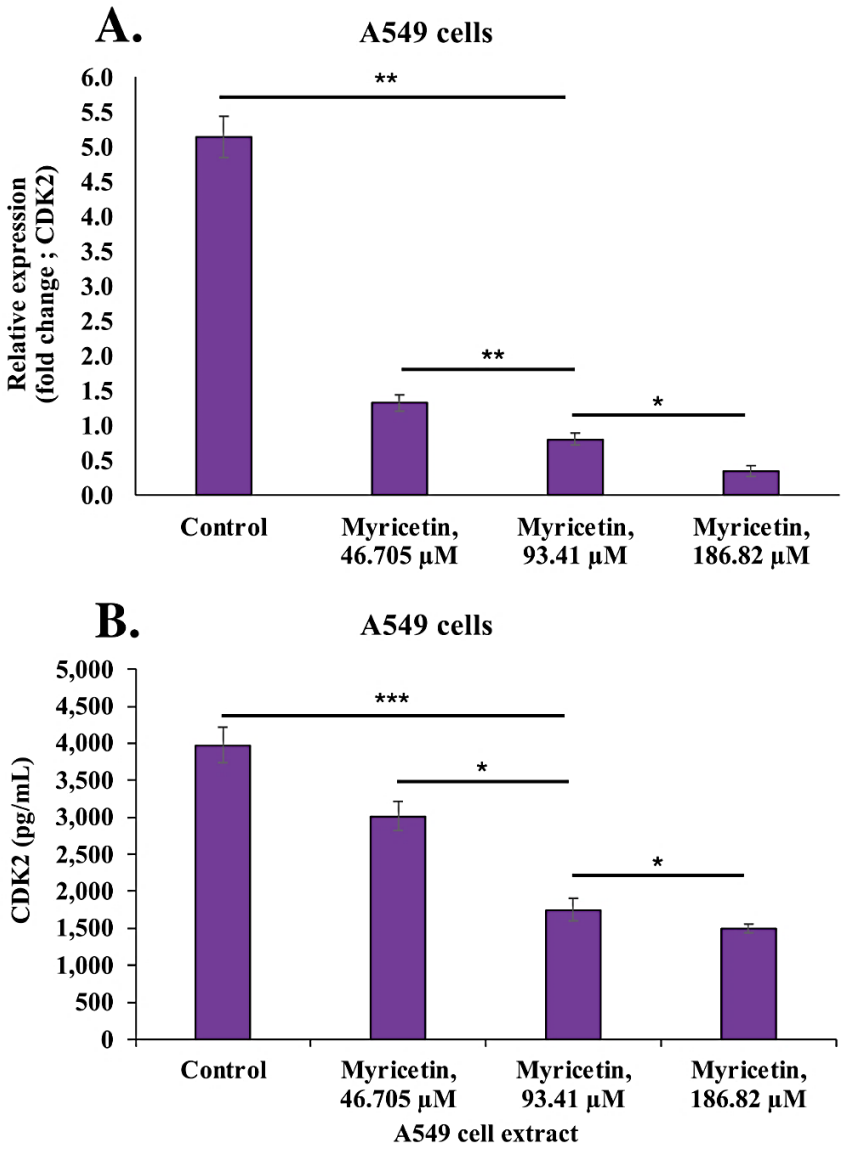


Figure 4: (A) Effect of half concentration of IC_{50} dose (46.705 µM), IC_{50} dose (93.41 µM), and double concentration of IC_{50} dose (186.82 µM) of Myricetin on the mRNA expression of CDK2 in A549 lung cancer cells (B) Result of half concentration of IC_{50} dose (46.705 µM), IC_{50} dose (93.41 µM), and double concentration of IC_{50} dose (186.82 µM) of myricetin on the activity level of CDK2 in A549 lung cancer cells.

While the findings of this study are favourable, several limitations must be addressed in future research. First, the *in vitro* results need to be validated *in vivo* using animal models to confirm myricetin's efficacy and safety profile in a physiological context. Second, the exact mechanisms underlying myricetin's cytotoxic effects, including its impact on apoptosis, autophagy, and other cell death pathways, require further investigation. Third, the potential for off-target effects and drug-drug interactions, particularly with cytochrome P450 enzymes, should be thoroughly evaluated.

CONCLUSION

In summary, this study highlights the potential of myricetin as a CDK2 inhibitor with significant anticancer activity against A549 lung carcinoma cells. Its dual mechanism of action, favourable ADMET properties, and diverse biological activity spectrum underscore its therapeutic potential. Future studies focusing on *in vivo* validation, mechanism elucidation, and structural optimization are essential to advance myricetin's development as a novel anticancer agent.

CONFLICT OF INTEREST

There is no conflict of interest among the author.

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ABBREVIATIONS

CDK2: Cyclin-dependent kinase 2; **ADMET:** Absorption distribution metabolism excretion and toxicity; **ELISA:** Enzyme-linked immunosorbent assay.

SUMMARY

Myricetin, a CDK2 inhibitor, has revealed momentous anticancer activity against A549 lung carcinoma cells, with potential for additional development through *in vivo* validation and structural optimization.

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