

Monotropein Inhibits Cell Growth and Induces Apoptosis in Breast Cancer MDA-MB-231 Cells

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ABSTRACT

Background: Breast cancer, a complex disease marked by the unregulated growth of atypical cells, is the most widely diagnosed malignancy in women globally, profoundly affecting public health. Breast cancer generally affects older women; however, it can also occur in younger persons. **Objectives:** The present study focused on investigating the anticancer effects of monotropein on breast cancer cells and elucidating its possible molecular targets through *in vitro* and *in silico* analyses. **Materials and Methods:** The MTT assay was utilized to study the cytotoxicity of monotropein on the growth of MDA-MB-231 cells. The cell damage and subsequent cytotoxicity caused by monotropein in breast cancer cells were studied using an LDH release assay kit. The concentrations of cyclin D1 in the control and monotropein-treated cells were evaluated using kits. Additionally, molecular docking studies were performed to predict potential interactions of monotropein with target proteins cyclin D1 and LDHA involved in cancer progression to understand the compound mechanisms. **Results:** The MTT assay findings demonstrated a significant reduction in MDA-MB-231 cell proliferation after treatment with various dosages of monotropein. The monotropein treatment caused cellular damage and cytotoxicity in MDA-MB-231 cells, as indicated by elevated LDH activity. Furthermore, the monotropein treatment markedly decreased the cyclin D1 in the breast cancer cells. Molecular docking predicted a stronger interaction between monotropein and LDHA (binding affinity = -6.4 kcal/mol; RMSD = 2.19 Å) than with Cyclin D1 (binding affinity = -5.9 kcal/mol; RMSD = 1.13 Å), suggesting LDHA as a potential direct target. The observed increase in LDH activity and concomitant reduction in Cyclin D1 expression support the hypothesis that monotropein suppresses cell proliferation mainly by interfering with cell-cycle progression, leading to cellular damage and apoptosis in MDA-MB-231 cells. **Conclusion:** The current findings demonstrate that monotropein treatment markedly suppresses proliferation and triggers apoptosis in MDA-MB-231 cells. Thus, it was apparent that monotropein could provide a beneficial natural compound for designing new therapeutic strategies against breast cancer. However, more experiments, including binding and enzyme kinetic assays, along with genetic perturbation (LDHA knockdown/rescue), are ultimately required to gain a deeper understanding of the mechanisms of monotropein.

Keywords: Lactate Dehydrogenase, Cellular Injury, Cytotoxicity, Monotropein, Molecular Docking, Breast Cancer.

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INTRODUCTION

Breast cancer, a multifaceted disease characterized by the uncontrolled proliferation of aberrant cells, remains the most widely diagnosed cancer in women globally, significantly

impacting public health. In 2020 alone, roughly 2.3 million women diagnosed with breast cancer, contributing to 685,000 fatalities globally.¹ This widespread incidence underscores its critical status as a predominant cause of cancer-associated deaths among females. The disease arises when normal cellular regulatory mechanisms are disturbed, such as failure of apoptosis, which allows abnormal or damaged cells to continue dividing uncontrollably and potentially metastasize to other bodily regions.² This biological heterogeneity necessitates a nuanced understanding of its various forms, as breast cancer is not a singular entity but rather a group of distinct diseases characterized by diverse molecular profiles and clinicopathological features.



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Globally, cancer is a predominant cause of deaths, accounting for nearly 10 million mortalities in 2020, with breast cancer contributing significantly to this burden, ranking among the top five deadliest cancer types.³ The fundamental cause of breast cancer progression involves abnormalities and irregularities in the normal cell cycle, alongside obstructed apoptosis signaling pathways. These cellular dysregulations often lead to the accumulation of genetic mutations, driving tumorigenesis and subsequent disease progression.⁴

The incidence of breast cancer, while primarily affecting older women, can also manifest in younger individuals. Indeed, while the most common demographic for breast cancer diagnosis is women between 50 and 69 years of age, there has been a recent trend indicating an increasing occurrence of the disease in women under 40. Despite significant advancements in breast cancer awareness and management, it remains the fifth leading cause of death in women worldwide, with alarmingly increased rates in nearly every region.⁵ Globally, breast cancer is the predominantly diagnosed cancer in females, and it is imperative to identify and understand the multifactorial elements contributing to its initiation and progression. This neoplastic condition involves a complex interplay of genetic predispositions, environmental causes, and lifestyle habits that collectively modulate cellular proliferation and differentiation within mammary tissues.⁶ Epidemiological data reveal distinct geographic and demographic disparities in breast cancer cases and mortality worldwide, reflecting the influence of varying risk factor profiles across populations. For instance, while developed nations exhibit higher incidence rates, developing countries often face a greater mortality burden due to delayed diagnosis and limited access to comprehensive care.⁷

Despite significant advancements in breast cancer therapy, various problems still persist, including the difficulty in optimizing drug dosages, managing adverse effects, and combating drug resistance, which collectively diminish patient quality of life and treatment efficacy. For instance, dose-limiting toxicities from certain inhibitors can cause severe adverse events in healthy tissues before any discernible impact on the tumor, thereby complicating the clinical development of new treatments.⁸ Furthermore, the development of multidrug resistance further impedes current cancer therapies, often leading to treatment failure due to cancer cells evolving mechanisms to evade therapeutic agents. This resistance can arise through diverse mechanisms, including mutations in drug targets or activation of alternative signaling pathways, highlighting the serious need for novel therapeutic strategies that can circumvent these acquired defense mechanisms.⁹ Monotropein is a bioactive iridoid glycoside compound extracted from the roots of *Morinda officinalis*. The diverse pharmacological effects of monotropein were reported previously, including its antioxidant,¹⁰ wound

healing,¹¹ anti-inflammatory,¹² and nephroprotective¹³ properties. Furthermore, monotropein showed anticancer activity against various cancers, such as colorectal cancer,¹⁴ lung cancer,¹⁵ and hepatocellular carcinoma.¹⁶ Apart from these biological activities, the anticancer mechanism of monotropein against breast cancer has not been reported yet. Therefore, the present study focused on evaluating the anticancer effects of monotropein on breast cancer cells, including *in silico* analyses.

MATERIALS AND METHODS

Chemicals

Monotropein, Fetal Bovine Serum (FBS), Dulbecco's Modified Eagle Medium (DMEM), antibiotics, and others were acquired from Sigma-Aldrich, USA. The test kits for quantifying the biochemical markers were acquired from Abcam, USA.

Cell culture

The breast cancer MDA-MB-231 cells were obtained from ATCC, USA, and cultivated in DMEM enriched with FBS (10%) and antibiotics (1%) in a CO₂ (5%) chamber. Cells were harvested upon reaching 80% confluency and utilized for subsequent analyses.

MTT cytotoxicity assay

The cytotoxicity of monotropein on the growth of MDA-MB-231 cells were investigated using MTT assay. Cells were cultivated on a 96-well plate for 24 hr. Consequently, the cells underwent monotropein treatment for an additional 24 hr at varying dosages of 2.5, 5, 10, 15, 20, 25, and 30 µM. Subsequent to the monotropein treatment, MTT (20 µL) and DMEM (100 µL) was mixed with each well for a duration of 4 hr. Finally, the absorbance was measured at 570 nm after dissolving the formed formazan deposits with 100 µL of DMSO and analyzed using an ELISA reader.

Lactate Dehydrogenase (LDH) release assay

LDH is a soluble enzyme leaked into the bloodstream upon cellular injury, serving as an indicator of cellular damage and toxicity. In this study, the release of LDH was employed to evaluate the cytotoxicity of monotropein on MDA-MB-231 cells. The cells were treated for 24 hours with diverse concentrations of monotropein (2.5-30 µM). After that, LDH activity was measured with the LDH Assay Kit (Elabscience, USA) as per the manufacturer's descriptions, with absorbance taken at 490 nm.

Analysis of cyclin D1 levels

The MDA-MB-231 cells from both control and treatment groups were gathered, and cell lysates were prepared using cell lysis buffer to quantify the cyclin D1. The levels of cyclin D1 was quantified in the cell lysates, utilizing the ELISA-based assay kits as per manufacturer's descriptions (Abcam, USA).

In silico analysis

The dataset retrieval for molecular docking analysis

Targets such as cyclin D1 (PDB ID: 6P8H)¹⁷ and LDHA (PDB ID: 4QSM)¹⁸ were retrieved from the Protein Data Bank (PDB) to perform the molecular docking analysis.

Preparation of protein structures and ligands

The protein structures of cyclin D1 and LDHA were pre-processed using Discovery Studio Visualizer (DSV) v19.1.0.18287 (www.accelerys.com). This involved removing water molecules and associated ligands, including cyclin-dependent kinase 4 and cyclin-dependent kinase inhibitor 1, as well as cyclin D1 and 3-[[7-(2,4-dimethoxypyrimidin-5-yl)-3-sulfamoylquinolin-4-yl]amino]benzoic acid, in conjunction with LDHA. The monotropein structure, obtained from the PubChem compound database in SDF format with 3D atomic coordinates provided, was then transformed into PDB format using DSV.¹⁹

Molecular docking and Visualization

The molecular docking process was performed for the defined targets, cyclin D1 and LDHA, with monotropein using Autodock Vina, built with an advanced scoring algorithm and integrated into PyRx software.²⁰ This process predicts the most favourable binding modes between the targets and the ligand.

The Autodock vina uses a new scoring mechanism,

$$C = \sum_{i < j} f_{titj}(r_{ij}),$$

C - Sum of intermolecular and intramolecular distance; Σ - Over all of the pairs of atoms; f_{titj} - Symmetric set of interaction functions; r_{ij} - Interatomic distance.

The defined targets cyclin D1, LDHA, and ligand monotropein have been converted into PDBQT format to carry out molecular docking studies. Using the PyRx virtual screening tool, we identified the active site residues interacting with the targeted biomarkers. Additionally, the properties of the grid box were assigned to cyclin D1 (size_x, y, z = 25 Å) and LDHA (size_x, y, z = 25 Å). After, the docked results were analysed using DSV to visualise the interactions with monotropein. The LigPlot*v2.2.9 was utilized to confirm the interactions between the cyclin D1-monotropein and LDHA-monotropein complexes.²¹

Statistical analysis

The statistical assays were performed using Graphpad Prism software, and data were given as Mean $\pm$ SD of triplicates. The data were scrutinized using One-way ANOVA and Tukey's *post hoc* test, with a significance set at $p < 0.05$.

RESULTS

In vitro

Monotropein treatment inhibits the viability of breast cancer MDA-MB-231 cells

The cytotoxicity of monotropein on the breast cancer MDA-MB-231 cell proliferation was evaluated using MTT assay, with findings depicted in Figure 1. The MTT test results suggest that monotropein treatment at varying dosages (2.5-30 μ M) markedly reduced the of MDA-MB-231 cell growth at dose-dependently. A notable decrease in breast cancer cell growth was seen after treatment with high dosages of monotropein. The IC_{50} value of monotropein against MDA-MB-231 cells were determined to be 15 μ M, which is subsequently utilized for future assays.

Monotropein treatment increases the LDH activity in MDA-MB-231 cells

The cytotoxic effects of monotropein on MDA-MB-231 cells were assessed by measuring LDH activity (Figure 2). The cells were subjected to various dosages of monotropein treatment for 24 hr, and LDH release was investigated with an LDH assay kit. Figure 2 demonstrates that monotropein treatment induced considerable cytotoxicity in breast cancer cells, as indicated by the increased LDH activity.

Monotropein treatment decreases the cyclin D1 levels in MDA-MB-231 cells

Figure 3 illustrates the levels of cell cycle regulator protein cyclin D1 in the control and monotropein-treated MDA-MB-231 cells. The control cells had elevated levels of cyclin D1. Simultaneously, the treatment of cells with 15 μ M of monotropein resulted in a substantial reduction in cyclin D1 when compared with the control group.

In silico

Molecular docking analysis cyclin D1 and LDHA revealed that monotropein exhibits better binding interactions with both targets. The resulting binding affinity, RMSD, and the types of bonds formed between the targets and monotropein were detailed in Table 1.

Cyclin D1

The monotropein interacted with the residues of cyclin D1, including GLU69, LYS180, GLN183 via the hydrogen bonds. Also, the hydrophobic residues such as LEU65, GLU75, PHE78, PRO79, THR184, VAL186, LEU188, and SER258 surrounded the cyclin D1-monotropein docked complex with the binding affinity of -5.9 kcal/mol and the RMSD of 1.125Å (Figures 4A, 4B and Table 1).

LDHA

The LDHA residues such as ALA98, ASN113, VAL136, ASN138, and THR248, interacted well with monotropein via the hydrogen bonds and the residues that include GLY29, VAL31, THR95, ALA96, GLY97, ARG99, LEU109, SER137, LEU143, LEU165, ALA238, ILE242, TYR247, and ILEU252, interacted via hydrophobic interaction, which helped to stabilize the complex further. The binding affinity was estimated as -6.4 kcal/mol, and the RMSD was observed as 2.191 Å (Figures 4C, 4D and Table 1).

The LigPlot⁺ was used to validate the interactions between the cyclin D1 and LDHA with the monotropein (Figures 4E, 4F). The analysis revealed that the hydrogen bonds were formed with the residues GLU69, LYS180, and GLN183, while hydrophobic interactions were observed with the residues LEU65, GLU75, THR184, ALA187, and LEU188. Similarly, the estimated LigPlot⁺ interactions confirmed that monotropein established seven hydrogen bonds with the residues ALA98, ASN113, VAL136,

ASN138, and THR248. Meanwhile, the residues such as THR95, GLY97, SER137, ILE242, TYR247, and ILE252 were involved in the hydrophobic interactions.

DISCUSSION

Breast cancer remains the most frequent malignancy in women globally, characterised by significant heterogeneity and complex tumorigenesis pathways. Despite advancements in awareness and management, it continues to be a primary cause of cancer-related mortality in females, responsible for nearly 15% of all cancer deaths.²² The disease is defined by the uncontrolled multiplication of abnormal cells within mammary tissue, often forming squamous cells that disregard normal cellular signaling for programmed cell death. This unregulated cellular growth can lead to tumor formation that, if malignant, may invade surrounding tissues or metastasize to distant anatomical sites.²³ The global increase in incidence rates, particularly in high-income countries, highlights the complex interplay of risk factors and

Table 1: Targets, PDB ID, binding affinity (kcal/mol), RMSD (Å), and their interacted residues with monotropein and its type of interactions.

Targets Name	Targets (PDB ID)	Binding affinity (Kcal/mol)	RMSD (Å)	Hydrogen bonds	Hydrophobic residues	Other types of bonds
Cyclin D1	6P8H	-5.9	1.125	GLU69, LYS180, GLN183	LEU65, GLU75, PHE78, PRO79, THR184, VAL186, LEU188, SER258	ALA187 ^{Alkyl}
LDHA	4QSM	-6.4	2.191	ALA98, ASN113, VAL136, ASN138, THR248	GLY29, VAL31, THR95, ALA96, GLY97, ARG99, LEU109, SER137, LEU143, LEU165, ALA238, ILE242, TYR247, ILEU252	-

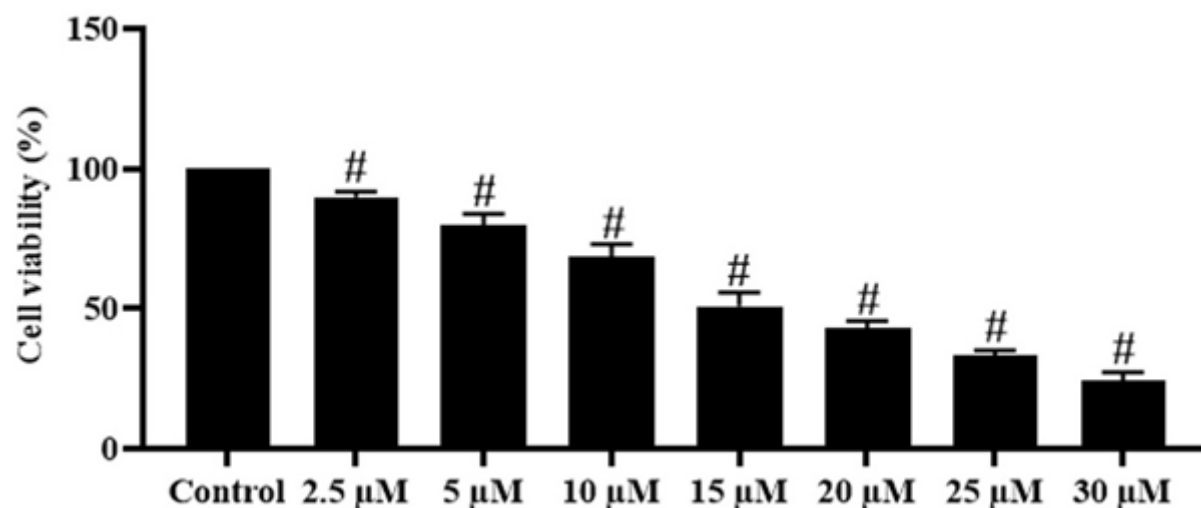


Figure 1: Effect of monotropein treatment on the viability of breast cancer MDA-MB-231 cells. The treatment with monotropein at various dosages (2.5–30 μM) remarkably suppressed the MDA-MB-231 cell viability in dose-dependent manner. The data were displayed as a Mean ± SD of triplicates. The data were evaluated statistically by one-way ANOVA and Tukey's *post hoc* test tests using GraphPad Prism software.

Note: '#' reveals that data were significantly differ at $p < 0.05$ from the control group.

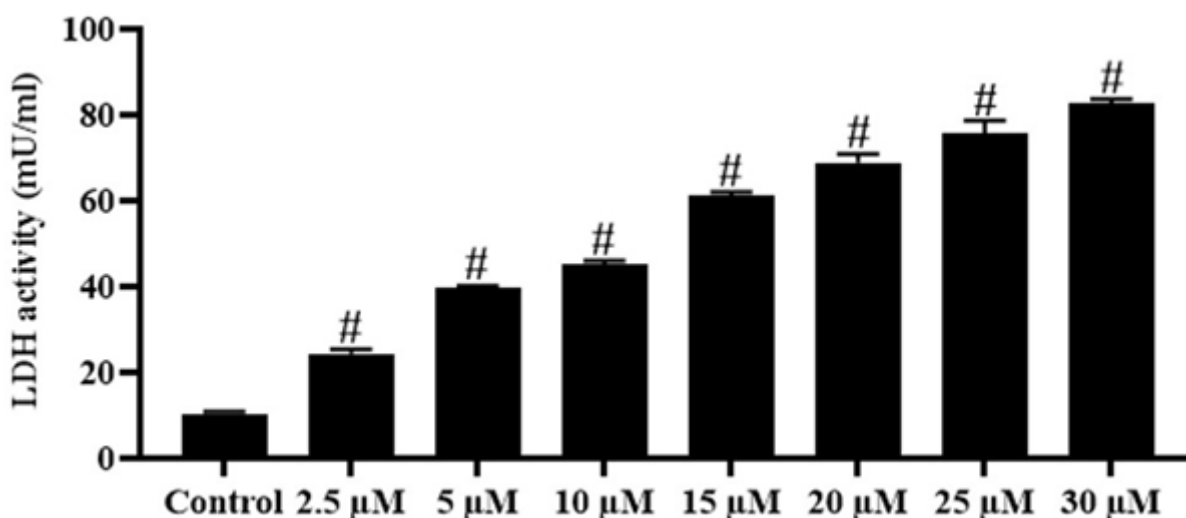


Figure 2: Effect of monotropein treatment on the LDH activity in MDA-MB-231 cells. The data were displayed as a Mean $\pm$ SD of triplicates. The data were evaluated statistically by one-way ANOVA and Tukey's *post hoc* test tests using GraphPad Prism software. Note: “#” reveals that data were significantly differ at $p < 0.05$ from the control group.

underscores the urgent need for enhanced preventive strategies. This global burden is further compounded by the fact that breast cancer accounts for 25% of all female cancers worldwide. Despite several improvements, breast cancer remains a challenging global health burden, demanding intensified research into its complex etiologies and the development of more effective therapeutic interventions.²⁴

The exploration of natural products, especially plant-derived bioactive compounds, has emerged as a hopeful avenue for identifying anticancer agents due to their diverse chemical structures and pharmacological properties. Despite their therapeutic potential, the clinical translation of many promising compounds faces hurdles, particularly concerning their selectivity towards cancerous cells over healthy tissues.²⁵ This challenge necessitates rigorous *in vitro* cytotoxic assessments to precisely quantify the differential impact of bioactive compounds on cancer cell viability versus normal cell viability. Consequently, detailed analyses comparing the cytotoxic effects on cancerous cells against those on normal cells are crucial for the early identification of compounds with a favorable therapeutic index, mitigating the risk of systemic toxicities.²⁶ The analysis of the effects of sample drug compounds on cancer cell viability is critical for identifying potential therapeutic agents and understanding their mechanisms of action. This process typically involves quantifying cell proliferation, cytotoxicity, or apoptosis in response to varying drug concentrations, often utilizing metrics like the IC_{50} index to compare treatment efficacy.²⁷ Furthermore, large-scale drug screens offer valuable data for understanding drug mechanisms, identifying cancer cell vulnerabilities, and facilitating the development of novel drugs and drug repurposing. This systematic approach allows for the functional investigation of cellular pathways underpinning drug sensitivity or resistance, thereby enabling a deeper understanding

of therapeutic responses. This analysis helps in distinguishing compounds with favorable therapeutic indices, thereby prioritizing those with a higher likelihood of clinical success and reduced side effects.²⁸ In the current work, the cytotoxicity of monotropein on breast cancer cells were evaluated using MTT assay. These findings revealed that the monotropein treatment noticeably diminished the MDA-MB-231 cell viability. Therefore, it was clear that monotropein can inhibit the development of breast cancer cells.

The LDH release assay is a widely recognized and robust method for quantifying cell viability and cytotoxicity, offering significant advantages in drug discovery and therapeutic efficacy evaluation.²⁹ This assay measures the activity of LDH, a stable cytoplasmic enzyme leaked into the cell culture supernatant upon plasma membrane injury, which is characteristic of cells undergoing necrosis, apoptosis, or other forms of cellular injury.³⁰ The presence of LDH in the extracellular milieu thus serves as a reliable biomarker for compromised cell membrane integrity, enabling the assessment of cell death in response to various stimuli, including potential drug compounds. This method is particularly valuable for screening drug candidates, as it can quantify the extent of cellular damage in a dose-dependent manner, providing critical insights into a compound's cytotoxic potential.³¹ Unlike assays that measure metabolic activity, the LDH assay directly quantifies membrane damage, providing a distinct advantage in differentiating between cytostatic and cytotoxic effects. This direct assessment of membrane integrity allows for precise evaluation of drug compound impact on cancer cells.³² In this study, the cytotoxic effects of monotropein on MDA-MB-231 cells were assessed by measuring LDH activity. The results demonstrate that monotropein treatment showed marked cytotoxicity in breast cancer cells, which is indicated by the increased LDH activity.

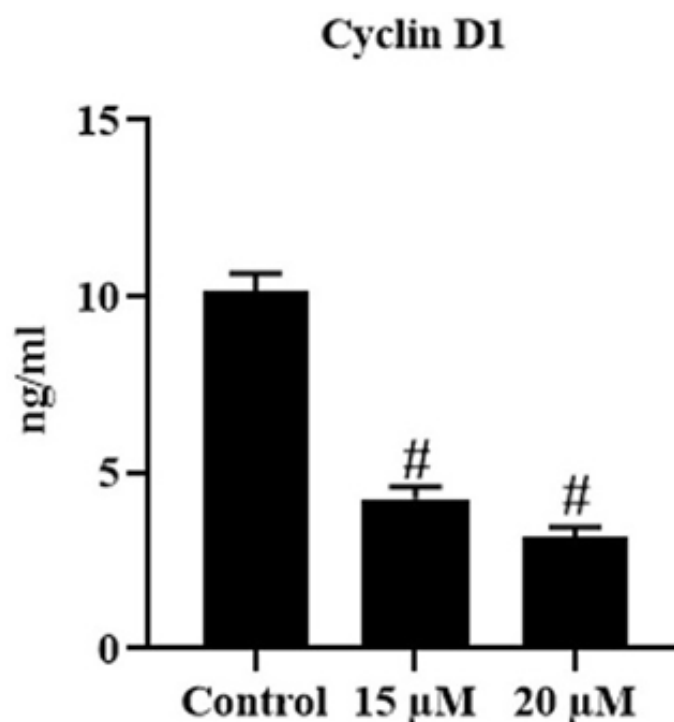


Figure 3: Effect of monotropein treatment on the cyclin D1 levels in the MDA-MB-231 cells. The data were displayed as a Mean $\pm$ SD of triplicates. The data were evaluated statistically by one-way ANOVA and Tukey's *post hoc* test tests using GraphPad Prism software. Note: '#' reveals that data were significantly differ at $p < 0.05$ from the control group.

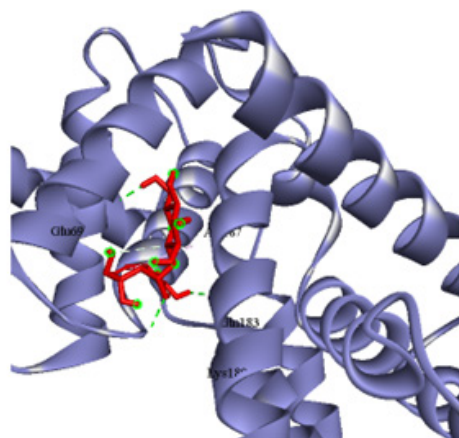
Cyclin D1 is an essential protein involved in cell cycle regulation and plays an essential role in promoting the transition from G1 to the S phase by associating with cyclin-dependent kinases 4 and 6. This interaction facilitates the phosphorylation of the retinoblastoma protein, resulting in the discharge of transcription factors and subsequent progression into DNA synthesis.³³ The CCND1 gene, encoding Cyclin D1, is often amplified in numerous human cancers, including up to 20% of breast cancers, highlighting its significance as an oncogene. In particular, nearly 15% of breast tumors exhibit CCND1 gene amplification, with over 50% demonstrating overexpression of the cyclin D1 protein.³⁴ This dysregulation, characterized by increased cyclin D1 levels, often emerges early in breast cancer pathogenesis, observed even in ductal carcinoma in situ and metastatic lesions. The oncogenic overexpression of cyclin D1 is frequently driven by genomic alterations such as gene amplification, where CCND1 is often the primary tumorigenic driver.³⁵ This amplification and subsequent overexpression contribute significantly to uncontrolled cellular proliferation, a hallmark of cancer, by dysregulating cell cycle progression. This proliferative advantage is often linked to a lower nutrient requirement in tumor cells with elevated cyclin D1 levels, further supporting their unchecked growth. Moreover, the aberrant upregulation of Cyclin D1 protein can lead to treatment resistance in breast cancer cells.³⁶ Therefore, targeting cyclin D1 may provide beneficial effects for breast cancer treatment. In a similar manner, the increased levels of cyclin D1 were observed in the MDA-MB-231 cells. Interestingly, the monotropein treatment markedly decreased the cyclin D1 levels in the breast cancer cells.

According to the *in vitro* findings, molecular docking studies were performed to explore the potential interactions between monotropein and its molecular targets, to elucidate the binding mechanisms underlying its anticancer activity against BC. Cyclin D1 and LDHA were selected as key targets owing to their essential involvement in regulating tumor cell proliferation and metabolic regulation, respectively. The *in silico* analysis revealed that monotropein binds stably to both the cyclin D1 and LDHA, with binding affinities of -5.9 kcal/mol and -6.4 kcal/mol, indicating favourable interaction energetics. The low RMSD values ($\leq 3.0 \text{ \AA}$) further support the stability of the complex. The observed *in vitro* downregulation of cyclin D1 in monotropein-treated cells aligns with these docking results, reinforcing the hypothesis that monotropein suppresses tumour proliferation by targeting cyclin D1, which could inhibit the G1 $\rightarrow$ S phase progression. Likely, monotropein established the hydrogen bonds with the residues specifically ALA98 of LDHA, which is located in the 3-{[7-(2,4-dimethoxypyrimidin-5-yl)-3-sulfamoylquinolin-4-yl]amino}benzoic acid binding site, indicating that potential interference of monotropein with this site leads to the metabolic disruption of LDHA enzymatic activity, thereby disrupting glycolytic metabolism and leakage of LDH observed experimentally.

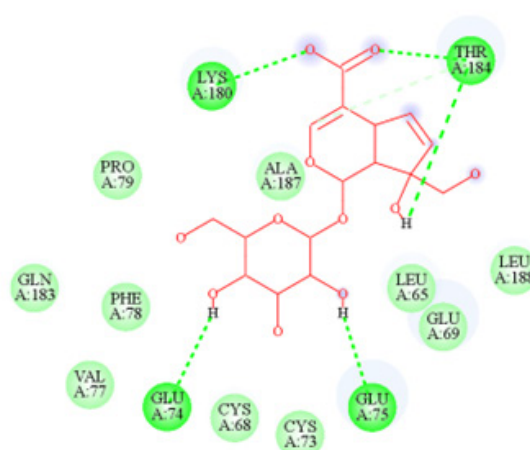
Visualization using LigPlot⁺ further validated these results, revealing multiple hydrogen bonds and hydrophobic interactions that stabilize both the cyclin D1-monotropein and LDHA-monotropein complexes. The abundance of these

Cyclin D1-Monotropein (PDB ID: 6P8H)

(A)

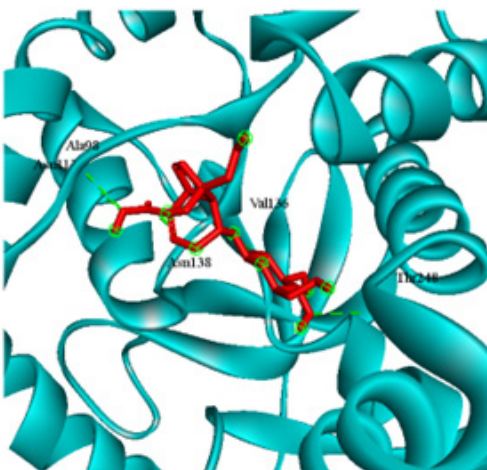


(B)

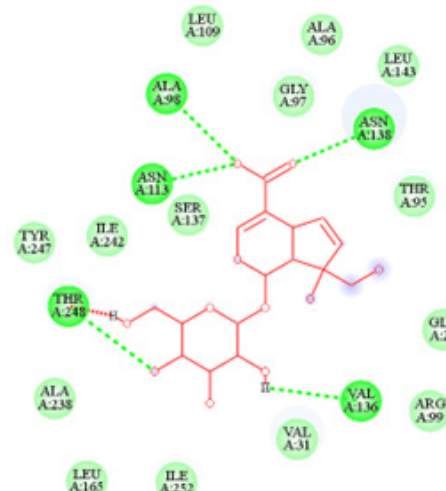


Lactate dehydrogenase A-Monotropein (PDB ID: 4QSM)

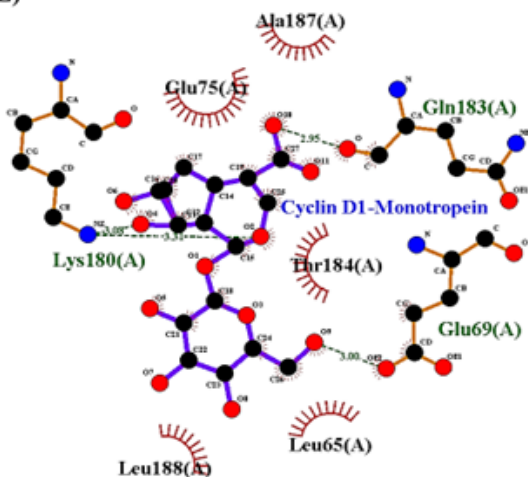
(C)



(D)



(E)



(F)

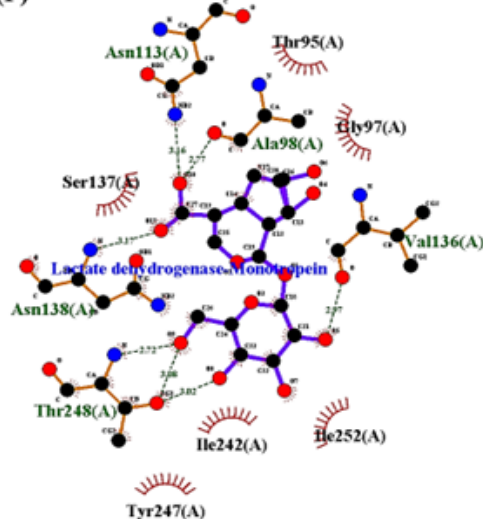


Figure 4: The docking poses of targets cyclin D1 and LDHA with the monotropein and its validation using LigPlot+. (A, B) The 3D and 2D docked poses of the Cyclin D1 with monotropein (C, D) The 3D and 2D docked poses of the Cyclin D1 with monotropein (E, F) The LigPlot+ validation for the Cyclin D1 and LDHA complex with the monotropein to confirm the hydrogen bonds.

interactions highlights the strong molecular interaction of monotropein with these targets. Collectively, the combined *in vitro* and *in silico* findings suggest that monotropein exhibits its anticancer effects via dual mechanisms. Firstly, the monotropein might directly bind to cyclin D1, resulting in its lower expression and inhibition of cell-cycle progression. Secondly, modulation of cancer cell metabolism, as evidenced by leakage of the LDHA from the cytosol to the medium, which reflects the process of apoptosis and necrosis.³⁶ Therefore, it was evident that monotropein treatment can inhibit uncontrolled cell proliferation in breast cancer cells via inhibiting cyclin D1 and leakage of LDHA.³⁷

CONCLUSION

The current findings demonstrate that monotropein treatment markedly suppresses proliferation and triggers apoptosis in MDA-MB-231 cells. The treatment with monotropein caused cellular damage, as indicated by elevated LDH activity and the induction of apoptosis in MDA-MB-231 cells. Also, the molecular docking study demonstrated that the monotropein exerted a better binding affinity with the cyclin D1 and LDHA, which may contribute to reduced cell proliferation, cell cycle arrest, and MDA-MB-231 cells death and subsequent release of LDH. Therefore, it was clear that monotropein has the promise to be a talented anticancer agent to manage breast cancer. However, further research is still required to clarify the specific molecular mechanisms involved in the anticancer effects of monotropein against breast cancer.

ABBREVIATIONS

CCND1 gene: Cyclin D1 gene; **FBS:** Fetal Bovine Serum; **DMEM:** Dulbecco's Modified Eagle Medium; **DMSO:** Dimethyl sulfoxide; **LDH:** Lactate Dehydrogenase.

FUNDING

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SUMMARY

Breast cancer is the most prevalent malignancy among women worldwide, distinguished by heterogeneity and intricate carcinogenesis pathways. Notwithstanding progress in knowledge and management, it remains a leading cause of cancer-related mortality in females. The present data indicate that monotropein administration significantly inhibits proliferation and induces apoptosis in breast cancer cells. The administration of monotropein resulted in cellular damage, as evidenced by increased LDH activity and the initiation of apoptosis in MDA-MB-231 cells. Consequently, it was evident that monotropein had potential as an effective anticancer drug for the treatment of breast cancer.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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