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Original Article

Crafting Cancer-Fighting Wonders: Synthesis, Characterization, and Evaluation of a Novel Thiazole Derivative Targeting EGFR

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ABSTRACT

Aim: The development of novel thiazole derivatives, namely PVS 3.1, 3.2, 3.3, and 3.4, marks a significant advancement in the field of anticancer drug discovery. These compounds were synthesized using an efficient, time-saving synthetic route that overcomes the limitations of conventional methods, which are often laborious, time-intensive, and costly. The new approach reflects a considerable step forward in the streamlining of drug development processes. **Materials and Methods:** The cytotoxic potential of the synthesized derivatives was systematically evaluated against two human cancer cell lines MCF-7 (breast adenocarcinoma) and A431 (epidermoid carcinoma of the lung) using the standard MTT assay. This colorimetric assay enabled the assessment of cell viability and revealed that all four compounds exhibited substantial inhibitory effects on cancer cell proliferation. The observed activity suggests promising antiproliferative properties inherent in the thiazole scaffold. **Results:** To further explore the molecular mechanism underlying the anticancer activity, the compounds were assessed for their inhibitory effect on the L858R/T790M double mutant form of the Epidermal Growth Factor Receptor (EGFR) tyrosine kinase. This specific EGFR mutation is commonly associated with acquired resistance to existing EGFR-targeted therapies and contributes significantly to uncontrolled cancer cell growth. Inhibitory activity of the PVS compounds against this mutant enzyme highlights their potential utility in overcoming resistance mechanisms and targeting key signaling pathways involved in tumor progression. **Discussion:** The findings suggest that the synthesized compounds exert a dual mode of action by both inducing cytotoxic effects in cancer cells and inhibiting a critical molecular target implicated in cancer development and drug resistance. Although these preliminary results are promising, further investigations including mechanistic studies, *in vivo* efficacy, toxicity profiling, and pharmacokinetic assessments are essential to fully establish the therapeutic potential of these thiazole derivatives. **Conclusion:** Overall, this study introduces a promising class of molecules with potential utility in the development of new anticancer therapies, particularly for treatment-resistant cancers. The dual-action capability of these compounds may offer a strategic advantage in designing multifaceted therapeutic approaches.

Keywords: Thiazole derivatives, Anticancer activity, MTT assay, EGFR tyrosine kinase, L858R/T790M mutation, Drug resistance, Cytotoxicity, Targeted therapy, Cancer cell lines, Dual-mode action.

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INTRODUCTION

Cancer remains one of the most challenging diseases of modern medicine, often associated with high morbidity and mortality. At its core, cancer is a disorder of uncontrolled cellular proliferation resulting from genetic and epigenetic alterations. Under physiological conditions, cellular growth, differentiation, and death are tightly regulated processes. However, in cancer, mutations within key regulatory genes disrupt this balance, enabling cells to bypass growth control mechanisms, evade apoptosis, and proliferate indefinitely. These aberrant cells may give rise to tumours, which are classified as benign or malignant. Malignant tumors are particularly dangerous due to their capacity to invade surrounding tissues and metastasize to distant organs.[1,2]

Cancer is not a singular disease but a multifactorial condition with diverse etiological contributors. Environmental factors, lifestyle choices, and genetic predisposition all interplay in cancer initiation and progression. Prolonged exposure to Ultraviolet (UV) radiation, for instance, has been implicated in DNA damage that leads to skin carcinogenesis. Carcinogenic compounds

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found in tobacco smoke represent another well-established risk factor, initiating mutations in oncogenes and tumor suppressor genes. Lifestyle-related factors, including high-fat diets, excessive alcohol intake, sedentary behaviour, and obesity, have been increasingly associated with elevated cancer risk. Additionally, hereditary syndromes resulting from germline mutations (e.g., BRCA1/BRCA2) contribute to susceptibility in specific cancer types.[3]

Recent studies have also highlighted the importance of metabolic pathways in carcinogenesis. In many instances, it is not the parent chemical compound but its metabolic by-products that exhibit carcinogenic potential. The biotransformation of certain xenobiotics by hepatic enzymes can yield reactive intermediates capable of inducing genetic damage.[4] Furthermore, hormonal imbalances are being investigated for their role in hormone-responsive cancers, including breast, ovarian, and prostate cancers. Endogenous and exogenous hormones, such as those influenced by reproductive history, contraceptive use, and hormone replacement therapy, may act as modulators in the tumorigenic process.[5]

Preventive strategies play a critical role in reducing cancer incidence. While a subset of cancers has a strong genetic component, many can be prevented through lifestyle modifications and minimizing exposure to known carcinogens. Public health education, routine screening, and early detection remain cornerstones in cancer control.

In conclusion, cancer represents a complex interplay of genetic, environmental, and metabolic factors. Ongoing research continues to elucidate novel mechanisms of pathogenesis and therapeutic targets. With a growing understanding of the disease and advances in molecular biology and pharmacology, the prospect of developing more effective prevention, diagnostic, and treatment strategies appears increasingly promising.

MATERIALS AND METHODS

Every scientific breakthrough starts in the lab, and the fight against cancer is no exception. Let's delve into the fascinating world of chemistry to see how these promising new compounds, PVS 3.1, 3.2, 3.3, and 3.4, were brought to life.

We use High-quality solvents and chemicals provided the building blocks, while Thin-Layer Chromatography (TLC) acted as a watchful eye, ensuring reactions progressed smoothly. Imagine TLC as a roadmap, guiding the scientists and revealing when the target compounds were formed. Once synthesized, the true identities of these compounds needed to be unraveled. Here's where powerful spectroscopic techniques came into play.

The synthesis and characterization of novel bioactive molecules constitute the foundational steps in the development of new therapeutic agents. In the present study, a series of thiazole derivatives, designated as PVS 3.1, 3.2, 3.3, and 3.4, were synthesized using high-purity reagents and solvents obtained from standard commercial sources. The progress of the reactions was monitored through Thin-Layer Chromatography (TLC), a rapid and efficient analytical method that enabled real-time assessment of reaction completion and product purity.

Following successful synthesis, comprehensive physicochemical and spectroscopic techniques were employed to elucidate and confirm the structural identities of the synthesized compounds. Initial characterization involved determination of melting points, which served as an essential parameter to assess compound purity and offer preliminary identification based on consistent thermal behaviour.

Infrared (IR) spectroscopy was subsequently utilized to identify characteristic functional groups within the synthesized molecules by analyzing their vibrational transitions. The presence of key functional moieties was inferred from specific absorption bands, corroborating the proposed structures.

Further structural validation was achieved using proton (1H) and carbon Nuclear Magnetic Resonance (NMR) spectroscopy. These spectra provided detailed insights into the electronic environment, chemical shifts, and connectivity of the atomic framework of the compounds. High-resolution NMR analyses were conducted at established instrumentation facilities, including the Bruker Avance system and the NMR facility at Savitribai Phule Pune University, ensuring high data fidelity and interpretative accuracy.

Mass Spectrometry (MS) was employed as a complementary technique to verify the molecular weights of the compounds and examine their fragmentation patterns. High-Resolution Mass Spectrometry (HRMS) further enhanced the precision of molecular mass determination, providing definitive confirmation of the molecular formulas.

The collective data obtained from these analytical techniques enabled unequivocal structural elucidation and purity confirmation of the synthesized thiazole derivatives. These well-characterized compounds are now positioned for further biological evaluation, particularly for their anticancer potential, as part of an ongoing investigation into targeted therapeutic development.[6]

The synthesis of novel triazole-thiazole hybrid derivatives involved a multi-step approach, beginning with the preparation of the key intermediate, 4-(4-chlorobenzyl)-1H-1,2,3-triazole. This compound was synthesized via a nucleophilic substitution reaction between 4-chlorobenzyl chloride and sodium azide in dichloromethane as the solvent. Equimolar quantities of the reactants were used, and the reaction was conducted at ambient temperature with continuous stirring. Thin-Layer Chromatography (TLC) was employed to monitor the reaction progress and confirm completion. Upon completion, the reaction

mixture was quenched using water or a dilute hydrochloric acid solution to neutralize unreacted sodium azide. The product was subsequently extracted using an appropriate organic solvent and purified through either recrystallization or column chromatography to yield the desired triazole intermediate.

In the subsequent step, the intermediate 4-(4-chlorobenzyl)-1H -1,2,3-triazole was subjected to esterification with 4-methyl-2-(p-tolyl)thiazole-5-carboxylic acid to yield the target compound, (1-benzyl-1H-1,2,3-triazol-4-yl)methyl 2-(4-bromophenyl) thiazole-5-carboxylate. The esterification reaction was carried out in Dimethylformamide (DMF), which served as a polar aprotic solvent to solubilize both reactants effectively. The carboxylic acid component was activated using a coupling agent, 4-Dimethylaminopyridine (DMAP), added in a 1:1 molar ratio relative to the acid, to facilitate nucleophilic substitution and promote ester bond formation.

The reaction mixture was maintained under continuous stirring at room temperature or slightly elevated temperature for a predetermined duration, allowing the esterification to proceed efficiently. Reaction progress was monitored by TLC. Upon completion, the mixture was quenched using a mild acidic solution to deactivate excess DMAP and remove byproducts. The crude product was then extracted using an organic solvent, followed by purification through recrystallization or column chromatography to obtain the pure ester derivative (Figure 1).

The novelty of the present study lies in the strategic integration of classical and advanced analytical techniques in the rational design, synthesis, and structural elucidation of a novel series of thiazole-based compounds (PVS 3.1-3.4) with potential bioactivity.

Specifically, the synthesis employed analytical-grade reagents and solvents, ensuring high chemical fidelity and reproducibility of the target compounds. The reaction progress was meticulously monitored using Thin-Layer Chromatography (TLC), not merely as a post-reaction verification tool, but as a real-time analytical approach to assess both reaction completion and product purity at each stage of the synthetic process. This dynamic application of TLC reflects an operational enhancement over conventional static monitoring and contributes to more efficient reaction optimization.

Following synthesis, the compounds were subjected to a hybrid characterization strategy, wherein melting point analysis served as an initial purity assessment and diagnostic parameter, while a suite of advanced spectroscopic techniques (e.g., NMR, IR, and mass spectrometry) was employed for definitive structural elucidation. This methodological synergy between classical thermal methods and high-resolution spectroscopic techniques provided robust validation of compound identity and structural integrity.

Furthermore, the novel molecular architecture of the synthesized thiazole derivatives introduces unexplored substitution patterns within the heterocyclic framework, potentially offering distinct pharmacological profiles that warrant further biological investigation. The deliberate design and systematic development of these novel scaffolds position the present work at the interface of synthetic innovation and therapeutic discovery, particularly in the context of anticancer drug development.[7]

This synthetic protocol, employing straightforward conditions and standard purification techniques, provided a reliable and efficient route to structurally novel triazole-thiazole conjugates. These hybrid scaffolds are of particular interest due to their potential pharmacological applications, especially in anticancer drug design. Synthesised Thiazole derivatives are summarized as follows in Table 1.

In vitro Pharmacological Activity

MTT Assay for Cell Viability Assessment

The *in vitro* cytotoxic potential of the synthesized compounds was evaluated against MCF-7 (human breast adenocarcinoma) and A431 (human epidermoid carcinoma) cell lines utilizing the standard MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide] assay. This colorimetric assay provides a reliable and sensitive approach to quantify cell viability, based on the metabolic reduction of MTT into formazan crystals by mitochondrial dehydrogenases in viable cells.

Initially, the cell lines were cultured under standard conditions in a suitable growth medium, and seeded into 96-well plates at a density of 1×10^4 cells per well in 100 µL volume. After 24 hr of incubation at 37°C with 5% CO_2 to allow for cell adherence and stabilization, the cells were treated with graded concentrations (20, 40, 60, 80, and 100 µg/mL) of the test compounds. Control groups included a blank (medium only) to evaluate background absorbance, and a vehicle control containing 0.2% DMSO in PBS to account for solvent-related effects. All treatments were performed in triplicate to ensure data accuracy and reproducibility.[8]

Following a 24-hr treatment period, the culture medium was aspirated and replaced with 20 µL of MTT solution (5 mg/mL in PBS). The assay relies on the ability of metabolically active cells to reduce the yellow tetrazolium dye into insoluble purple formazan. After an additional 4-hr incubation period under the same environmental conditions, the presence of formazan crystals was confirmed microscopically as an indicator of viable, metabolically active cells.[9]

To solubilize the formazan crystals, 200 µL of DMSO was added to each well, followed by a 10-min incubation at 37°C in the dark (aluminum foil-wrapped plates) to prevent photodegradation of the chromogenic product. The optical density of the resulting purple solution was measured at 550 nm using a microplate reader. A higher absorbance value corresponded to greater cell viability,

whereas a reduction in absorbance indicated a dose-dependent cytotoxic effect of the test samples.

The inclusion of appropriate controls enabled accurate interpretation of the cytotoxic effects by differentiating them from baseline cellular behavior and solvent interference.[10] This methodological approach allowed for robust evaluation of the antiproliferative efficacy of the synthesized compounds, setting the groundwork for further mechanistic studies and *in vivo* validation.

EGFR Inhibition Mechanism of Action

Signaling, Activation, Dimerization and Transduction

The Epidermal Growth Factor Receptor (EGFR), a member of the ErbB family of receptor tyrosine kinases, plays a pivotal role in regulating cellular processes such as proliferation, differentiation, survival, and migration. EGFR is a transmembrane glycoprotein characterized by an extracellular ligand-binding domain, a single hydrophobic transmembrane segment, and an intracellular tyrosine kinase domain.

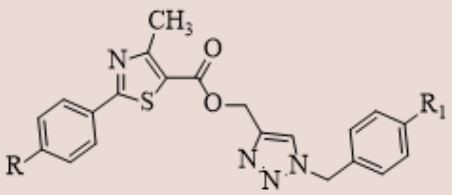
EGFR activation is initiated upon binding of specific ligands, including Epidermal Growth Factor (EGF) and Transforming Growth Factor-alpha (TGF-α), to its extracellular domain. Ligand engagement induces a conformational change that facilitates receptor dimerization. EGFR can form either homodimers (EGFR-EGFR) or heterodimers with other members of the HER/ErbB family, such as HER2/neu (ErbB2), HER3 (ErbB3), or HER4 (ErbB4).

Receptor dimerization activates the intrinsic tyrosine kinase domain, leading to trans-autophosphorylation of specific tyrosine residues within the cytoplasmic tail of the receptor. These phosphorylated tyrosines serve as docking sites for various adaptor and signaling proteins containing Src Homology 2 (SH2) or phosphotyrosine-binding (PTB) domains, thereby initiating multiple downstream signaling cascades (Figure 2).[11]

RESULTS

A series of novel thiazole-based compounds (PVS 3.1 to PVS 3.4) were successfully synthesized (Table 1). Evaluated for their physicochemical, spectroscopic, cytotoxic, and enzymatic properties. All synthesized thiazole derivatives were obtained in good yields, ranging from 68% to 91%. The melting points were uncorrected and found to be in the range of 188°C to 234°C. The compound PVS 3.2 exhibited the highest percentage yield (91%), while PVS 3.3 showed the lowest (68%) (Table 2). The compounds were characterized by IR, NMR, and mass spectrometry: IR spectra confirmed the presence of characteristic functional groups, such as carbonyl (C=O) stretching (e.g., around 1513-1655 cm^{-1}), aromatic C=C stretching (~1430-1490 cm^{-1}), and C-H stretching in both methyl and aromatic regions.

Table 1: Synthesized Thiazole Derivatives.

Sl. No.	Compound Code	R Group and R_1 Group	Core structure
1.	PVS 3.1	4-bromophenyl	
2.	PVS 3.2	4-fluorophenyl, 4-ethylbenzyl	
3.	PVS 3.3	4-fluorophenyl, 4-methylbenzyl	
4.	PVS 3.4	p-tolyl, 4-chlorobenzyl	

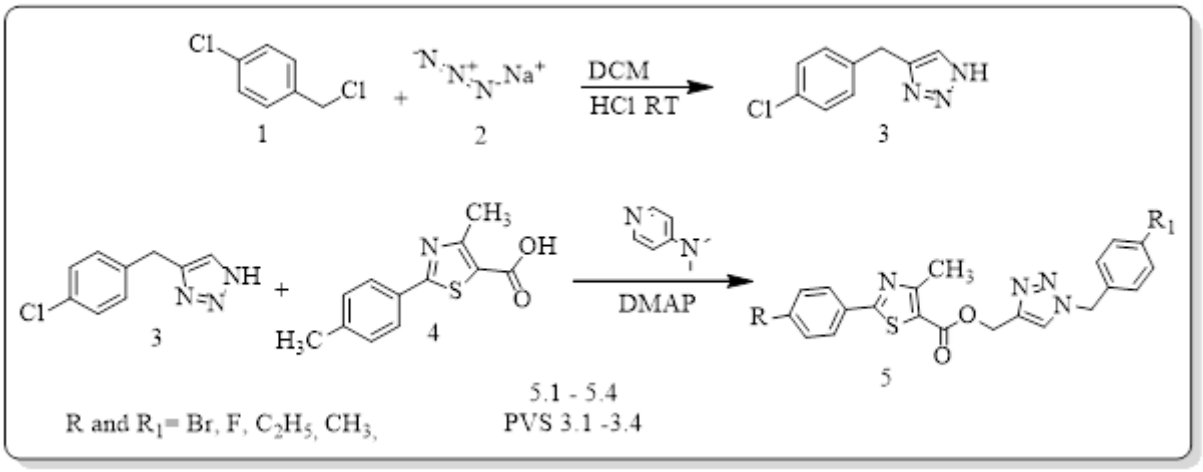


Figure 1: Method for the synthesis of thiazole derivatives.

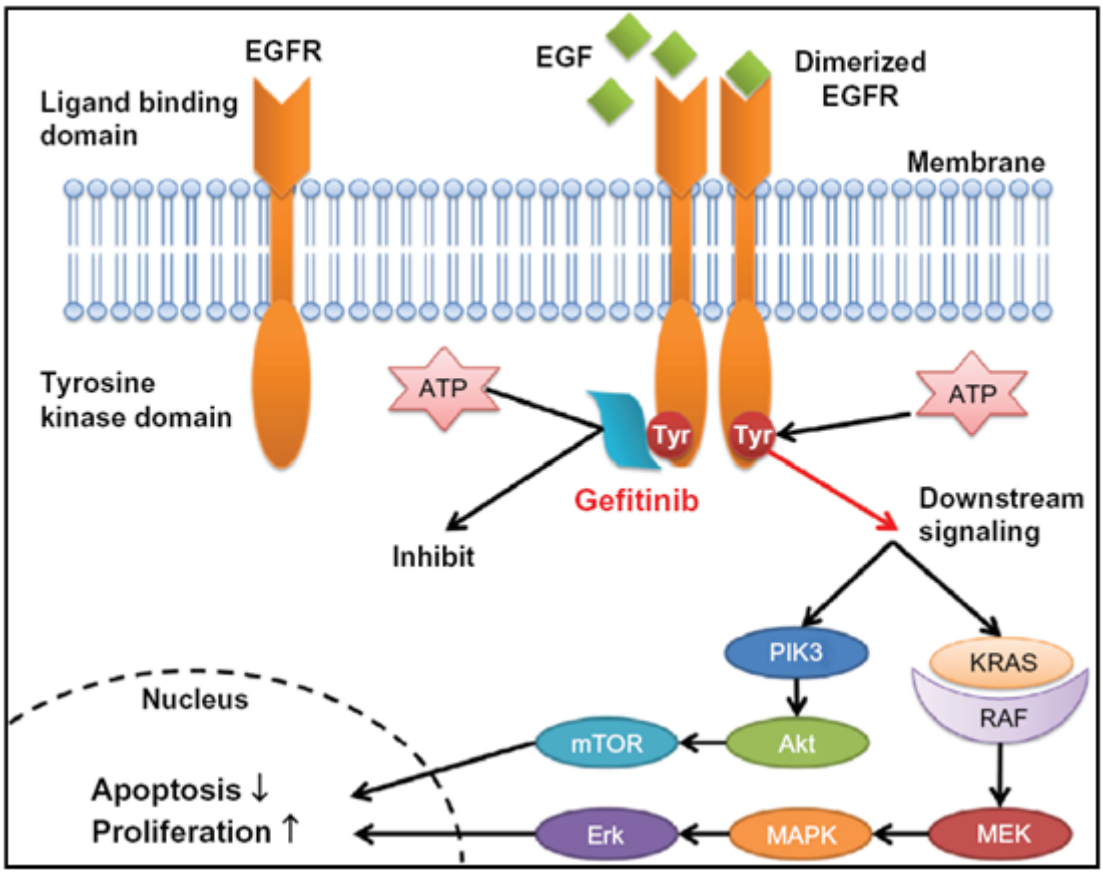


Figure 2: Epidermal Growth Factor Receptor Inhibition Pathways.[11]

^{1}H NMR spectra showed aromatic proton signals between δ 6.89-7.88 ppm, while the methylene protons adjacent to the triazole and ester functionalities appeared between δ 5.39-5.51 ppm. Mass spectra (*m/z*) confirmed the molecular ion peaks of the compounds, with molecular weights matching the expected values (e.g., PVS 3.1: 455.0, PVS 3.2: 435.0, PVS 3.3: 423.0, PVS 3.4: 439.0) (Table 3).[12] The synthesized thiazole derivatives were tested for their *in vitro* anticancer potential using the MTT assay on MCF-7 (human breast cancer) and A431 (human lung cancer) cell lines. PVS 3.4 exhibited the strongest cytotoxicity, with an IC_{50} value of 310 µg/mL against MCF-7 and 58.59 µg/mL against A431 cells. PVS 3.3 also showed significant inhibition, particularly against MCF-7 cells (IC_{50}=490 µg/mL). PVS 3.1 and PVS 3.2 were less potent, with higher IC_{50} values, indicating comparatively weaker activity. These findings suggest that the structural variations in the R and R1 substituents significantly influence anticancer activity (Table 4).[13,14]

EGFR Tyrosine Kinase Inhibition

To explore the potential mechanism of action, the compounds were tested for their ability to inhibit EGFR (Epidermal Growth Factor Receptor) tyrosine kinase, particularly the 1M17 mutant form associated with lung cancer. Only PVS 3.4 demonstrated notable enzymatic inhibition, achieving 64% inhibition of EGFR activity in an ELISA-based assay. In contrast, the reference inhibitor dasatinib exhibited only 26% inhibition under the same conditions. Other compounds (PVS 3.1, PVS 3.2, and PVS 3.3) did not show significant EGFR inhibition. These results suggest that PVS 3.4 may exert its potent anticancer activity by targeting EGFR tyrosine kinase (Table 5).[15,16]

DISCUSSION

Evaluation of Novel Thiazole Derivatives for Anticancer Activity Using MTT and EGFR Activity Assays

The investigation into the anticancer potential of newly synthesized Thiazole derivatives was undertaken through MTT and EGFR enzymatic activity assays, following standard cell-based and biochemical evaluation protocols.

MTT Assay for Cytotoxicity Evaluation

The MTT assay, a colorimetric technique that measures cellular metabolic activity as an indicator of cell viability, proliferation, and cytotoxicity, was employed to assess the effects of the Thiazole derivatives. The assay principle relies on the ability of viable cells to reduce the yellow tetrazolium salt (MTT) into insoluble purple formazan crystals via mitochondrial dehydrogenase enzymes. The intensity of the developed color, measured

spectrophotometrically, is directly proportional to the number of metabolically active cells.[15,16]

In the present study, human breast cancer (MCF-7) and lung cancer (A431) cell lines were selected as experimental models. Cells were seeded into 96-well plates and allowed to adhere. Following incubation, various concentrations of Thiazole derivatives (PVS 3.1, PVS 3.2, PVS 3.3, and PVS 3.4) were introduced, and the cells were incubated for 24 hr. Subsequently, MTT reagent was added, and after further incubation, the resulting formazan crystals were dissolved in DMSO, and absorbance was recorded at 570 nm using a microplate reader (Figure 3).[17]

Results and Interpretations

The Thiazole derivatives demonstrated varying degrees of cytotoxicity. Among them, PVS 3.4 and PVS 3.3 exhibited potent antiproliferative activity against MCF-7 cells, with IC_{50} values of 310 µg/mL and 490 µg/mL, respectively. Compounds PVS 3.2 and PVS 3.1 showed moderate cytotoxic effects, with IC_{50} values of 580 µg/mL and 850 µg/mL, respectively. These results suggest that PVS 3.4 and PVS 3.3 possess superior efficacy in inhibiting breast cancer cell growth compared to their counterparts.

Extending the evaluation to A431 lung cancer cells, PVS 3.4 and PVS 63.25 exhibited significant cytotoxicity, achieving IC_{50} values of 58.59 µg/mL and 63.25 µg/mL, respectively. PVS 3.3 displayed moderate inhibitory effects, whereas PVS 3.2 did not demonstrate significant activity on the A431 cell line.

EGFR mutations, notably L858R, in the progression of lung cancer, the most active compound, PVS 3.4, was evaluated using an *in vitro* enzymatic assay specifically targeting the L858R/1M17 EGFR mutant tyrosine kinase. PVS 3.4 achieved a substantial 64% inhibition of kinase activity. This degree of inhibition is notably higher than that of dasatinib, a known tyrosine kinase inhibitor, which has been reported to inhibit EGFR activity by approximately 26% in similar enzymatic contexts. The pronounced inhibition

Table 2: Physical Constant and Percentage Yield of synthesized Thiazole molecules.

Sl. No.	Comp. Code	R Group	Melting Point Uncorrected	Percentage Yield
1	PVS 3.1	4-bromophenyl	188^{0}C-192^{0}C	82
2	PVS 3.2	4-fluorophenyl, 4-ethylbenzyl	230^{0}C-234^{0}C	91
3	PVS 3.3	4-fluorophenyl, 4-methylbenzyl	210^{0}C-214^{0}C	68
4	PVS 3.4	p-tolyl, 4-chlorobenzyl	194^{0}C-198^{0}C	74

Table 3: Spectroscopical Data.[12]

Sl. No.	Compound Code	IR (cm -1)	NMR δ [ppm]	Mass m/z (M^+H)
1.	PVS 3.1 (1-benzyl-1H-1,2,3 -triazol-4-yl)methyl 2-(4-bromophenyl) thiazole-5-carboxylate	1513.29 (C=O, Streching, M). 1429.43(Aromatic, C=C, Streching), 2920.36 (C-H, Streching, M.), 3082.50 (C-H str., aromatic).	6.19-7.88 Aromatic (a-e) {09 H}; 5.40 (f) {2 H}; 5.47 (g) {2H}; 2.75 (h) {2H}	455.0
2.	PVS 3.2 (1-(4-ethylbenzyl)-1H-1 ,2,3-triazol-4-yl)methyl 2-(4-fluorophenyl)-4-methylthiazole-5-c arboxylate	1515.16 (C=O, Streching, M). 1435.02 (Aromatic, C=C, Streaching), 2920.40 (C-H Streching, aromatic)	6.89-7.83 Aromatic (a-e) {09 H}; 5.39 (f) {2 H}; 5.47 (g) {2H}; 3.80 (h) {2H}	435.0
3.	PVS 3.3 (1-(4-methylbenzyl)-1H-1 ,2,3-triazol-4-yl)methyl 2-(4-fluorophenyl)-4-methylthiazole-5-c arboxylate	1507.70 (C=O, Streching, M). 1436.88 (Aromatic, C=C, Streching), 2916.64 (C-H, Streching, M), 3117.91 (C-H Streching, aromatic).	7.05-7.83 Aromatic (a-e) {09 H}; 5.41 (f) {2 H}; 5.51 (g) {2H}; 2.74 (h) {2H}	423.0
4.	PVS 3.4 (1-(4-chlorobenzyl)-1H-1 ,2,3-triazol-4-yl)methyl 4-methyl-2-(p-tolyl) thiazole-5-carboxylate	1654.90 (C=O, Streching, M). 1490.90 (Aromatic, C=C, Streching), 2920.36 (C-H, Streching, M), 3117.91 (C-H Streching, aromatic).	7.22-7.83 Aromatic (a-e) {09 H}; 5.41 (f) {2 H}; 5.51 (g) {2H}; 2.39 (h) {2H}	439.0

Table 4: Evaluation of the cytotoxic effects of the synthesized compounds (Scheme 3) on MCF-7 and A431.[13,14]

Comp. Code	R	R_1	MCF-7 Human Breast Cell Line (IC_{50} µg/mL)	MCF-7 Human Breast Cell Line (IC_{50} µg/mL) (Ref. value)	A431 Human Lung Cell Line (IC_{50} µg/mL)	A431 Human Lung Cell Line (IC_{50} µg/mL) (Ref. value)
PVS 3.1	-Br	-H	850	>200	63.25	>50
PVS 3.2	- F	$-C_2H_5$	580	>210	NA	>80
PVS 3.3	-F	$-CH_3$	490	>180	77.56	>70
PVS 3.4	$-CH_3$	-Cl	310	>205	58.59	>80

Table 5: Anti-proliferative activity, *in vitro* enzymatic activity (EGFR Activity) assay screened synthesized compounds.[15,16]

Comp. Code	R	R_1	Enzymatic activity (% Inhibition) Human EGFR (1M17) Elisa
PVS 3.1	-Br	-H	------
PVS 3.2	- F	$-C_2H_5$	------
PVS 3.3	-F	$-CH_3$	------
PVS 3.4	$-CH_3$	-Cl	64.00
Dasatinib[17] (Standard)	-----	-----	26.00[17]

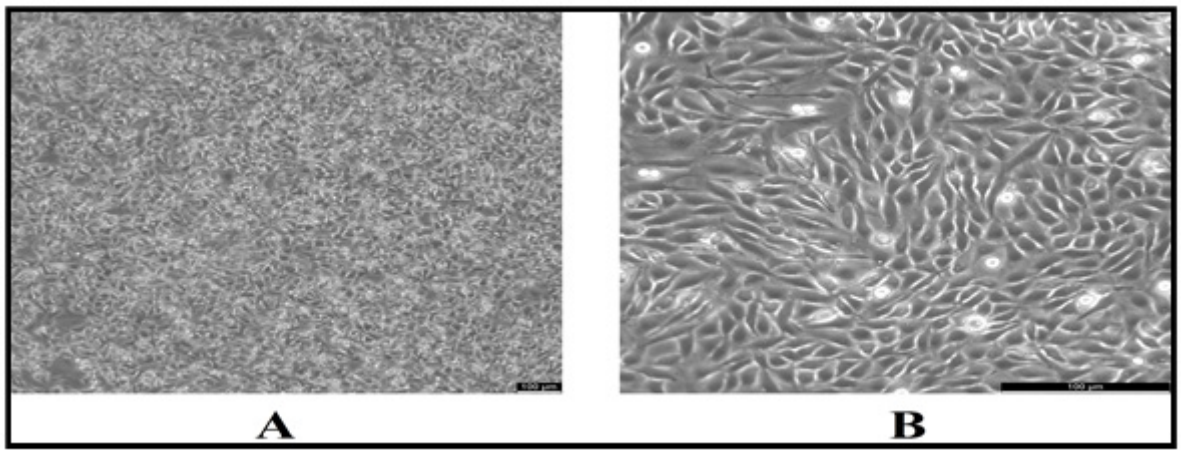


Figure 3: *In vitro* cell cytotoxicity of formulations on Breast cells a) control, b) 100 (µg/mL) PVS 3.4.[17]

by PVS 3.4 indicates a potentially robust mechanism of action through the interference of EGFR-dependent signaling pathways essential for tumor cell growth and survival.

CONCLUSION

The exploration of novel Thiazole derivatives for their anticancer properties has led to the identification of promising candidates with significant therapeutic potential. Among the synthesized compounds, PVS 3.4 and PVS 3.3 demonstrated strong antiproliferative effects against the MCF-7 human breast cancer cell line, suggesting their efficacy in targeting hormone-responsive malignancies. In particular, PVS 3.4 stood out for its enhanced cytotoxic activity, supporting its selection for further mechanistic investigations.

Extending the evaluation to human lung carcinoma cells (A431), compounds PVS 3.4 and PVS 63.25 exhibited notable growth inhibition, highlighting their effectiveness across multiple cancer models. These findings suggest the potential versatility of Thiazole derivatives in targeting distinct cancer cell types.

To gain deeper insight into the mechanism of action, PVS 3.4 was further examined for its effect on Epidermal Growth Factor Receptor (EGFR) tyrosine kinase activity, specifically the L858R/1M17 mutant variant commonly implicated in non-small cell lung cancer. The compound exhibited a substantial 64% inhibition of EGFR enzymatic activity *in vitro*. This inhibitory efficacy notably surpasses that of dasatinib, a well-characterized tyrosine kinase inhibitor, which demonstrates approximately 26% inhibition under comparable assay conditions. The marked suppression of mutant EGFR signaling by PVS 3.4 provides a

plausible explanation for its potent cytotoxicity in lung cancer models and supports its potential as a targeted therapy candidate.

This study underscores the promising therapeutic potential of newly synthesized Thiazole derivatives, especially PVS 3.4, which demonstrated marked cytotoxic effects in breast (MCF-7) and lung (A431) cancer cell lines along with a superior EGFR tyrosine kinase inhibition profile when compared to dasatinib. The significantly higher inhibitory activity observed for PVS 3.4 (64%) versus dasatinib (26%) supports its candidacy for further mechanistic exploration and preclinical development as a targeted anticancer agent.

FUTURE FINDINGS

In this study, a series of new thiazole derivatives (PVS 3.1-3.4) were synthesized and thoroughly characterized. Their anticancer activities were tested using the MTT assay on MCF-7 (breast cancer) and A431 (lung cancer) cell lines. Among the compounds, PVS 3.4 and PVS 3.3 showed strong growth-inhibiting effects on MCF-7 cells, which represent hormone-sensitive breast cancer.

Further testing on A431 lung cancer cells revealed that PVS 3.4 and PVS 63.25 significantly reduced cell growth. Notably, PVS 3.4 was the most effective compound, displaying potent cytotoxic effects on both cancer cell lines.

PVS 3.4 works, its ability to block the Epidermal Growth Factor Receptor (EGFR) tyrosine kinase enzyme was examined, focusing on the mutant L858R/1M17 form linked to lung cancer. PVS 3.4 inhibited EGFR activity by 64%, which was much higher than the 26% inhibition seen with dasatinib, a known tyrosine kinase inhibitor. This suggests that the strong anticancer effects of PVS 3.4 may be due to its ability to block EGFR activity.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

MCF-7: Michigan Cancer Foundation-7 (Human breast cancer cell line); **NMR:** Nuclear Magnetic Resonance; **MASS:** Mass Spectrometry; **MTT:** 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide; **EGFR:** Epidermal Growth Factor Receptor; **IR:** Infrared Spectroscopy; **DMSO:** Dimethyl Sulfoxide.

SUMMARY

This study explored the potential of novel thiazole compounds (PVS 3.1-3.4) as anticancer agents. The compounds were successfully synthesized and characterized. Functional assays revealed promising anti-cancer activity against human cancer cell lines. These findings highlight the promising therapeutic potential of these thiazole compounds. Further investigation is warranted to elucidate their mechanisms of action and assess their efficacy *in vivo* models. This research paves the way for the development of novel therapeutic strategies in the fight against cancer.

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