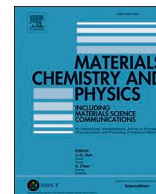




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## Integrated experimental and computational insights into thiazolidine derivatives with potent cytotoxicity against PC-3 prostate cancer cells

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## HIGHLIGHTS

- **A<sub>4</sub>** (4-Cl) and **A<sub>5</sub>** (4-Br) outperform standards (Darolutamide/R-Bicalutamide) against PC-3 cells, that induce **p53/p21 upregulation** (24-fold) triggering cell cycle arrest/apoptosis.
- **Electron-withdrawing halogens** enhance reactivity and target affinity.
- **Conserved pharmacophores** with optimal H-bond distances (2.06–2.18 Å, POM analysis).
- High GI absorption, zero Lipinski violations, no mutagenicity (ADME/Osiris).
- **A<sub>4</sub>/A<sub>5</sub>** exhibit superior bioavailability vs. nitro-analogs (**A<sub>3</sub>**).

## ARTICLE INFO

## Keywords:

Thiazolidine derivatives  
PC3  
DFT  
Molecular docking  
ADME/POM analysis

## ABSTRACT

In this study, a new series of 3-Acetyl-2-phenyl-5,5-dimethylthiazolidine-4-carbohydrazide (**A<sub>1-6</sub>**) was synthesized and comprehensively characterized by FT-IR, <sup>1</sup>H/<sup>13</sup>C NMR, and mass spectrometry. The cytotoxic potential of the compounds was evaluated in vitro against PC-3 human prostate cancer cells using the MTT assay. Among the series, compounds **A<sub>4</sub>** and **A<sub>5</sub>**, bearing 4-chlorophenyl and 4-bromophenyl groups, respectively, exhibited the most potent cytotoxicity with IC<sub>50</sub> values of 50.65 ± 0.98 µg/mL and 50.03 ± 0.98 µg/mL, closely comparable to standard drugs Darolutamide (55.4 ± 0.9 µg/mL) and R-Bicalutamide (80.34 ± 0.89 µg/mL). In contrast, the least active compound **A<sub>6</sub>** which incorporate 4-methylphenyl group exhibited an IC<sub>50</sub> of 120 ± 0.83 µg/mL. Gene expression analysis confirmed that these compounds induced significant upregulation of tumor suppressor genes *p53* and *p21*, indicating a mechanism of cell cycle arrest and apoptosis. Density Functional Theory (DFT),

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<https://doi.org/10.1016/j.matchemphys.2025.131256>

Received 17 April 2025; Received in revised form 3 June 2025; Accepted 7 July 2025

Available online 11 July 2025

0254-0584/© 2025 Published by Elsevier B.V.