Original Article | Published: 03 March 2023

Evaluation of N^{10}-substituted acridone-based derivatives as AKT inhibitors against breast cancer cells: in vitro and molecular docking studies

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3 Biotech **13**, Article number: 111 (2023)

Abstract

A series of N^{10}-substituted acridone-2-carboxamide derivatives were synthesized and evaluated for their potent anti-cancer agents targeting AKT kinase. In vitro cytotoxicity activity of the target compounds was tested against breast cancer cell lines (MCF-7 and MDA-MB-231). Among the tested compounds, four compounds (**7f**, **8d**, **8e**, and **8f**) exhibited promising anti-cancer activity against both cancer cell lines. Notably, compound **8f** demonstrated the highest activity against MCF-7 and MDA-MB-231 at IC_{50} values of 4.72 and 5.53 µM, respectively. In vitro AKT kinase activity revealed that compounds **7f** and **8f** were the most potent AKT inhibitors with IC_{50}

values of 5.38 and 6.90 μM, respectively. In addition, the quantitative ELISA method of testing confirmed that compound **8f** effectively inhibited cell proliferation by suppressing the activation of p-AKT Ser^{473}. Furthermore, molecular docking studies revealed that compound **8f** can bind well to the active site of the AKT enzyme. The in silico ADME studies suggested that all synthesized molecules showed good oral bioavailability with a low-toxicity profile and can be used for further optimization as AKT kinase inhibitors in the treatment of breast cancer.

Data availability

The data used to support the findings of this study are included within the manuscript.

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Acknowledgements

The authors are grateful to the Department of Health Research (DHR), Government of India, New Delhi, Grant/Award Number: no. V.25011/547-HRD/2016-HR for providing funding for research.

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Contributions

TTY contributed to the study conduction, synthesis, data collection, analysis and interpretation of results, and draft/manuscript preparation; PDP was involved

in the synthesis and data collection; GMS performed the molecular docking and data collection; MSK assisted in the methodology suggestions for biological studies, suggestions, and supervision, writing—reviewing and editing, and critical review of the manuscript; MC reviewed, edited, and critically revised the manuscript; MYC contributed to the conceptual design, reviewing and editing, and approval of the final version. All authors reviewed the results and approved the final version of the manuscript.

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Ethics declarations

Conflict of interest

The authors declare that there is no conflict of interest.

Research involving human participants and/or animals:

The authors confirm that there is no involvement of human participants and/or animals in conducting research.

Informed consent

Not applicable.

Supplementary Information

Below is the link to the electronic supplementary material.

Supplementary file1 (DOCX 11242 KB)

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Cite this article

Yadav, T.T., Patil, P.D., Shaikh, G.M. *et al.* Evaluation of N^{10}-substituted acridone-based derivatives as AKT inhibitors against breast cancer cells: in vitro and molecular docking studies. *3 Biotech* **13**, 111 (2023). https://doi.org/10.1007/s13205-023-03524-z

Received	Accepted	Published
24 November 2022	13 February 2023	03 March 2023

DOI

https://doi.org/10.1007/s13205-023-03524-z

Keywords

Acridone-2-carboxamide **AKT**

Molecular docking **Anti-cancer** **SAR**

Breast cancer