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# 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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## 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  $\mu$ M, 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  $\mu\text{M}$ , 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<sup>473</sup>. 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.

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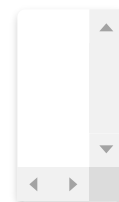
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## Data availability

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

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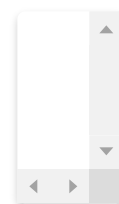
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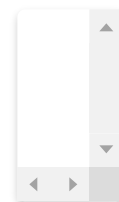
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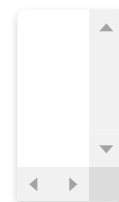
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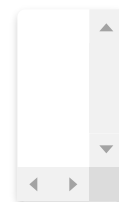
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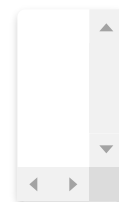
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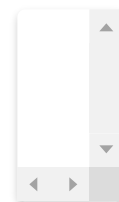
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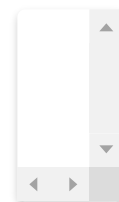
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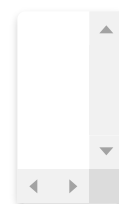
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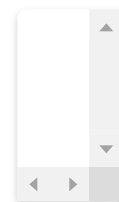
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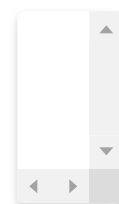
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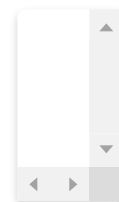
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### Contributions

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

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### Conflict of interest

The authors declare that there is no conflict of interest.

Research involving human participants and/or animals:

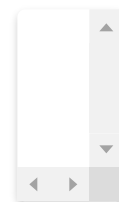
The authors confirm that there is no involvement of human participants and/or animals in conducting research.

Informed consent

Not applicable.

## Supplementary Information

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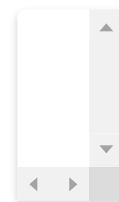
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