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Synthesis, cytotoxicity, and docking based analysis of acridone-*N*-acetamides as AKT kinase inhibitors

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Abstract

The primary goal of this study is to synthesize and characterize *N*-substituted Acetamido derivatives of acridone, where the acetamido moiety has been considered a linker which is crucial for several biological activities, including anti-cancer activity. In this context, the anti-proliferative activity of synthesized derivatives was evaluated against human breast (MCF-7, MDA-MB-231), lung (A-549), and skin (A-431) cancer cell lines. Results revealed that compounds **8 h**, **8i**, **9 h**, and **9i** showed the most potent activity against MCF-7 cell lines with IC_{50} values of **13.96 µM**, **8.25 µM, 9.45 µM,** and **6.76 µM,** respectively. In addition, all these compounds were found to be non-toxic against normal cells (NIH/3T3). Further, AKT kinase

inhibition assay results showed that compounds **8i** and **9i** have the efficacy to inhibit the AKT kinase with potential anti-cancer activity. The cell cycle analysis revealed that compounds **8i** and **9i** could arrest the G_0/G_1 phase of the cell cycle and absorption titration with CT-DNA identified that these molecules could interact with DNA. In order to understand the drug-likeness properties, all the compounds were evaluated by various in silico screening, and these compounds exhibited optimal physicochemical features as excellent lead molecules. Finally, in vitro results were validated using a molecular docking study, which revealed binding interactions in the active site of AKT.

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Ethics declarations

Conflict of interest

The authors declare that they have no known competing financial interests.

Additional information

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Supplementary file1 (DOCX 7186 KB)

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