

**أبحاث جامعة سيناء المنشورة
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Design, synthesis and biological screening of some diaryl acetamide derivatives as potential cytotoxic agents on HL-60(TB) cell line

Bioorganic Chemistry • Article • 2025 •

DOI: 10.1016/j.bioorg.2025.108999



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Abstract

In this study, novel diaryl acetamide derivatives were designed and evaluated as potential cytotoxic agents against the leukemic cells HL-60

(TB) with tyrosine kinase FMS-3(FLT-3) enzyme inhibitory activity. The designed molecules were synthesized and investigated for the FLT3 enzyme inhibition. Compounds 5a, 15b, and 16b showed significant inhibitory activity against the FLT-3 enzyme. Assessment of cytotoxicity on HL-60 cells revealed that compound 15b exhibited superior activity than Quizartinib (AC220). Additionally, compounds 5a and 15b effectively arrested the cell cycle at the G₁ phase upon testing on HL-60 cells, suggesting potential abilities in blocking HL-60 cells' proliferation. The annexin-V stain assay demonstrated that compounds 5a, 15b, and 16b induced apoptosis in HL-60 cells. Furthermore, the ELISA assay showed that the blocking of cell cycle proliferation of HL-60 cells was mediated via the induction of cell cycle regulatory proteins p53 and p21. Meanwhile, the observed apoptosis induction was mediated by increasing apoptotic mediators, Bax/Bcl-2 ratio, and up-regulating caspase-3. Molecular docking studies revealed the binding affinities and interactions of the newly synthesized compounds, along with the reference compound Quizartinib, with the FLT-3 enzyme binding site. © 2025 Elsevier Inc.

Author keywords

Diaryl acetamide; Dimedone; FLT-3 kinase inhibitors; HL-60 (TB); Leukemia; Oxadiazole; Quizartinib; Thiazole; Triazole

Indexed keywords

EMTREE drug terms

2 [[4 (4 chlorophenyl)thiazol 2 yl)amino] n [4 [(5,5 dimethyl 3 oxocyclohex 1 en 1 yl)amino]phenyl]acetamide; 2 [[5 (4 chlorophenyl) 1,3,4 oxathiazol 2 yl)thio] n [4 [(5,5 dimethyl 3 oxocyclohex 1 en 1 yl)amino]phenyl]acetamide; 2 [[5 (4 chlorophenyl) 4 phenyl 4h 1,2,4 triazol 3 yl)thio] n [4 [(5,5 dimethyl 3 oxocyclohex 1 en 1 yl)amino]phenyl]acetamide; 5,5 dimethyl 1,3 cyclohexanedione; acetamide derivative; antineoplastic agent; caspase 3; cytotoxic agent; diaryl acetamide derivative; Flt3 ligand; protein Bax; protein bcl 2; protein p21; protein p53; quizartinib; unclassified drug

EMTREE medical terms

alkylation; antineoplastic activity; antiproliferative activity; Article; binding affinity; carbon nuclear magnetic resonance; controlled study; drug design; drug screening; drug synthesis; enzyme binding; enzyme inhibition; enzyme linked immunosorbent assay; flow cytometry; G1 phase cell cycle checkpoint; HL-60 cell line; human; human cell; in vitro study; molecular docking; proton nuclear magnetic resonance

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5,5 dimethyl 1,3 cyclohexanedione	126-81-8
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Funding text 2

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- ☐ Alshaya, D.S. (1)
- ☐ Alshehri, M. (1)
- ☐ Althobaiti, A. (1)
- ☐ El-Bedewy, D.A.A.Z. (1)
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