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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
protein bcl 2	219306-68-0

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Funding text 2

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☐ Hegazy, M.M. (4)☐ Ramadan, M.F. (3)☐ Abd Al-Latif, S.F. (1)☐ Abdel Salam, K. (1)☐ Abdel-Azeem, M.A. (1)[View more](#)

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☐ 10	Introduction to Natural Remedies in Disease Management and Treatment (Book Chapter)	Hegazy, M.M., Ramadan, M.F.	2025	<i>Natural Remedies in Disease Management and Treatment</i> pp. 1-25	0
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☐ 2	Technology-enhanced compression and AI-integrated lymphedema care: a narrative review	Atiaa, A.G., Mostafa, M.M., Ellakwa, D.E.-S.	2025	Irish Journal of Medical Science Article in Press	0
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☐ 8	Comparative study between calcium gluconate with diosmin, cabergoline, and cabergoline with diosmin in prevention of ovarian hyperstimulation syndrome in high-risk women undergoing intracytoplasmic sperm injection (ICSI) procedures	Abdallah, A.M., Hussien, A.K., Alarfaj, S.J., (...), Mosbeh, M.H., Sadek, E.M.	2025	Frontiers in Pharmacology 16,1655866	0
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Ashry, M., Ali, F.K., Gadelmawla, M.H.A., (...), Ali, O.K., Askar, H.

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Abdelsattar, D.E., Elaraby, A., Naguib, H.M., (...), Zaki, E.G., El-Meligy, A.B.

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Egyptian Journal of Petroleum 34(4), pp. 333-346

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- ☐ Ashour, A.M. (2)
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- ☐ Khames, A. (2)
- ☐ Abdel Daim, Z.J. (1)
- ☐ Abdelkader, N.A. (1)
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- ☐ Abumansour, I.S. (1)
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☐ 3	Harnessing Nature for Breast Cancer Management: Effects of Fisetin-Loaded Nigellasomes Embedded in Microneedles Improve Tumor Suppression and Reduce Oxidative Stress	Elhabal, S.F., Mohammed Ali, E., Hababeh, S., (...), Fouad, M.A., Mohsen Elsaid Hamdan, A.	2025	Pharmaceutics 17(11),1392	0
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☐ 4	Hepatoprotection by Methylene Blue Against Doxorubicin Toxicity Through Coordinated Modulation of Oxidative Stress, ER Stress, and Apoptotic Pathways <i>Open Access</i>	Gad, E.S., Ashour, A.M., Gad, A.M., (...), Gadelmawla, M.H.A., Mansour, M.	2025	Pharmaceutics 18(11),1625	0
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☐ 2	Multifunctional chromium–yttrium modified sodium-borate glasses with enhanced optical stability and gamma-ray shielding for photovoltaic and radiation protection applications	Sadeq, M.S., Alsaiani, F.M., Al-Bassami, N.S., (...), Alshamari, A., Abdo, M.A.	2026	Radiation Physics and Chemistry 241,113519	0
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☐ 3	Absorber enhancement strategies in solar stills: A comprehensive review on thermodynamic, material, and sustainability perspectives	Ramzy, K., Alawad, M.A., abdelAziz, E.A., (...), Bassyouni, M., Kabeel, A.E.	2026	Separation and Purification Technology 385,136358	0
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☐ 4	Advances and challenges in sustainable solar desalination for freshwater production	Ramzy, K., Elbatal, I., Almetwally, E.M., (...), Bassyouni, M., Kabeel, A.E.	2026	Solar Energy 304,114190	0
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☐ 5	Ligand field modulation via Mn2+ /Ni2+ exchange in heavy metal borate glasses across Vis–NIR range	Almunyif, A., Siddiq, H., Aljuraide, N.I., (...), Abul-Magd, A.A., Elkelany, E.A.	2025	Journal of Alloys and Compounds 1049,185415	0
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☐ 7	Association between Nitric Oxide Production in Preeclampsia and Variations in the Endothelial Nitric Oxide Synthase Gene <i>Open Access</i>	Noah, W.E., Oraby, E.A., El-Moneim, M.A.A., (...), Elsaid, A.M., El-Taweel, H.M.A.	2025	Journal of South Asian Federation of Obstetrics and Gynaecology 17(5), pp. 603-611	0
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☐ 9	Natural bioactive compounds and herbal medicines targeting common signaling pathways in endometriosis: mechanisms and therapeutic implications	Elbanna, A.H., El-Dessouki, A.M., Mageed, S.S.A., (...), El-Shiekh, R.A., Hamdy, S.A.	2025	Naunyn Schmiedeberg S Archives of Pharmacology Article in Press	0
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