



Design and Evaluation of Antimicrobial Activity of New Pyrazoles, 1,2,4-Triazole and 1,3,4-Thiadiazol Derivatives Bearing 1,4-Dihydroquinoxaline Moiety

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Abstract—An effective method for synthesizing a series of fifteen new compounds Ethyl 3-(2-(3-amino-1,4-dihydroquinoxaline-2-carbonyl)hydrazono)butanoate (**II**), 3-amino-N'-benzylidene-1,4-dihydroquinoxaline-2-carbohydrazide derivatives (**IV-VI**), phenyl-4-oxothiazolidin-3-yl)-1,4-dihydroquinoxaline-2-carboxamide derivatives (**VII-IX**), 3-(3-amino-1,4-dihydroquinoxalin-2-yl)-5H-[1,2,4]triazolo[3,4-a]isoindol-5-one (**X**), 1,4-dihydroquinoxaline-2-carbonyl)-N-substituted hydrazine carbothioamide (**XI-XII**), 5-(3-amino-1,4-dihydroquinoxalin-2-yl)-4-substituted -4H-1,2,4-triazole-3-thiol (**XIII-XIV**) and 5-(3-amino-1,4-dihydroquinoxalin-2-yl)-N-substituted -1,3,4-thiadiazol-2-amine (**XV-XVI**) based on 1,4-dihydroquinoxaline moiety in 60-85 % yields starting from reaction of hydrazide 3-Amino-1,4-dihydroquinoxaline-2-carbohydrazide (**I**) with ethyl acetoacetate has been proposed. The designed compounds have been successfully screened *in-vitro* for their antibacterial and antifungal activities. Structural identifications of the obtained products have been carried out by spectroscopic techniques including FTIR, ¹H NMR, ¹³C NMR, and mass spectroscopy. The relation between the structure of the synthesized compounds and their activity against selected bacteria and fungi was studied and favorable results were obtained. The majority of tested compounds showed moderate antibacterial activities except compound 3-amino-N-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)-1,4-dihydroquinoxaline-2-carboxamide (**VIII**) that notably exhibited the most potent antibacterial activity against the tested *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* bacteria. Further antifungal studies indicated that the compounds Ethyl 3-(2-(3-amino-1,4-dihydroquinoxaline-2-carbonyl)hydrazono)butanoate (**II**), 3-amino-N-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)-1,4-dihydroquinoxaline-2-carboxamide (**VIII**), 3-amino-N-(2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl)-1,4-dihydroquinoxaline-2-carboxamide (**IX**) and 2-(3-amino-1,4-dihydroquinoxaline-2-carbonyl)-N-phenyl hydrazine carbothioamide (**XI**) exerted the highest antifungal activities against *Aspergillus flavus* and *Candida albicans* fungi.

Keywords: pyrazole, quinoxaline, carbohydrazide, thiadiazoles, antibacterial, antifungal

REFERENCES

1. Appelbaum, P.C., Hunter, P.A., *Int. J. Antimicrob. Agents.*, 2000, vol. 16, pp. 5–15. doi 10.1016/s0924-8579(00)00192-8

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2. Ball, P., *J. Antimicrob. Chemother.*, 2000, vol. 46, pp. 17–24. doi 10.1093/oxfordjournals.jac.a020889
3. Desai, N.C., Pandya, D., Vaja, D., *Med. Chem. Res.*, 2017, vol. 27, pp. 1–9. doi 10.1007/s00044-017-2040-5
4. Lu, X., Liu, X., Wan, B., Franzblau, S.G., Chen, L., Zhou, C., You, Q., *Part 2 Eur. J Med. Chem.*, 2012, vol. 49, pp. 164–171. doi 10.1016/j.ejmech.2012.01.007
5. Carey, J.S., Laffan, D., Thomson, C., Williams, M.T., *Org. Biomol. Chem.*, 2006, vol. 4, pp. 2337–2347. <https://doi.org/10.1039/B602413K>
6. Bailly, C., Echeperre, S., Gago, F., Waring, M., *J. Anti.Cancer Drug Des.*, 1999, vol. 14, pp. 291–303.
7. Teja, R., Kapu, S., Kadiyala, S., Dhanapal, V., Raman, A. N., *J. Saudi. Chem. Soc.*, 2016, vol. 20, pp. 387–392. <https://doi.org/10.1016/j.jscs.2012.12.011>
8. El-Ashry, E.S.H., Abdel-Rahman, A.A.H., Rashed, N., Rasheed, H. A., *Pharmazie.*, 1999, vol. 54, pp. 893–897.
9. Peraman, R., Kuppusamy, R., Killi, S.K., Reddy, Y.P., *Int. J. Med. Chem.*, 2016, vol. 2016, pp. 1–8. <https://doi.org/10.1155/2016/6471352>
10. El-Atawy, M.A., Hamed, E.A., AlHadi, M., Omar, A.Z., *Molecules*, 2019, vol.24, 4198, pp. 1-16. doi 10.3390/molecules24224198
11. Brock, E.D., Lewis, D.M., Yousaf, T.I., Harper, H.H., U.S. Patent WO 9951688, 1999.
12. Carta, A., Loriga, M., Paglietti, G., Mattana, A., Fiori, P.L., Mollicotti, P., Sechi, L., Zanetti, S., *Eur. J. Med. Chem.*, 2004, vol. 39, pp. 195–203. <https://doi.org/10.1016/j.ejmech.2003.11.008>
13. Burguete, A., Pontiki, E., Hadjipavlou-Litina, D., Ancizu, S., Villar, R., Solano, B., Moreno, E., Torres, E., Pérez, S., Aldana, I., Monge, A., *Chem. Biol. Drug. Des.*, 2011, vol. 77, pp. 255–267. Doi 10.1111/j.1747-0285.2011.01076.x
14. Gihsoy, A., Terzioglu, N., Otuk, G., *Eur. J. Med. Chem.*, 1997, vol. 32, pp. 753–757.
15. Rollas, S., Gulerman, N., Erdeniz, H., *Farmaco.*, 2002, vol. 57, pp. 171–174. doi 10.1016/s0014-827x(01)01192-2
16. Dikio, C.W., Okoli, B.J., Mtunzi, F.M., *Cogent. Chem.*, 2017, vol. 3, pp. 1–14. doi 10.1080/23312009.2017.1336864
17. Lekshmy, R.K., Thara, G.S., *AIP Conf. Proc.*, 2014, vol. 1620, pp. 230–234. <https://doi.org/10.1063/1.4898246>
18. El-Faham, A., Farooq, M., Khattab, S.N., Elkayal, A.M., Ibrahim, M.F., Abutaha, N., Wadaan, M.A., Hamed, E.A., *Chem. Pharm. Bull.*, 2014, vol. 62, pp. 591–599. doi 10.1248/cpb.c14-00143
19. Holla, B.S., Poorjary, K.N., Rao, B.S., Shivananda, M.K., *Eur. J. Med. Chem.*, 2002, vol. 37, pp. 511–517. doi 10.1016/s0223-5234(02)01358-2
20. Yousif, E., Majeed, A., Al-Sammarræ, K., Salih, N., Salimon, J., Abdullah, B., *Arabian. J. Chem.*, 2013, vol. 10, pp. 1639–1644. doi 10.1016/j.arabjc.2013.06.006
21. Elkanzi, N.A.A., Ghoneim, A.A., Hrichi, H., *Chem. J. Mold*, 2019, vol. 14, pp. 105–116. Doi 10.19261/cjm.2019.638
22. Hrichi, H., Elkanzi, N.A.A., *R.J.L.B.P.C.S.*, 2018, vol. 4, pp. 690–706. doi 10.26479/2018.0406.55
23. El Azab, I.H., Elkanzi, N.A.A., Gobouria, A.A., *J. Heterocyclic. Chem.*, 2018, vol. 55, pp. 65–76. doi 10.1002/jhet.2978
24. Komykhov, S.A., Ostras, K.S., Kostanyan, A.R., Desenko, S.M., Orlov, V.D., Meier, H., *J. Heterocycl. Chem.*, 2005, vol. 42, pp. 1111–1116. <https://doi.org/10.1002/jhet.5570420612>
25. NCCLS., *Approved standard NCCLS M38-A., National Committee for Clinical Laboratory Standards.*, Wayne, 2002.