

Unveiling the Efficacy of 3-Hydrazinoquinoxaline-2-Thiol Against *Pseudomonas aeruginosa*

Jawahir A. Mokhtar*, **, ***** (MD, PhD), Dalya Attallah** (MD), Mona Abdulrahman Alqarni*, (MD, PhD), Tariq Ekhmimi*, (MD, MSc), Bandar Hasan Saleh*, **, (MD, PhD), Hanouf A. Niyazi*, (MD, PhD), Hatoun A. Niyazi*, (MD, PhD), Noof R. Helmi*, (PhD) Hussam Daghistani***, *****, (MD, PhD), Yousef Almoghribi***, *****, (MD, PhD), Khalil Alkuwaity****, *****, (PhD), Ahmad M Sait****, *****, (PhD), Mohammed Mufrih****, *****, (PhD), Mazen A. Ismail****, (MD, SBFM, ArBFM, MedEd), Ohood S Alharbi*****, (MD, PhD), Wafaa Alhazmi****, (PhD), Abdelbagi Alfadil *, *****, (MD, PhD), Karem Ibrahim* (MD, PhD),

ABSTRACT

Pseudomonas aeruginosa (*P. aeruginosa*) is a serious opportunistic pathogen, especially in immunocompromised individuals and those with cystic fibrosis. Its ability to acquire resistance poses challenges in clinical settings. *P. aeruginosa* has increasingly developed resistance to the last-resort antibiotics. Repurposing, also known as drug repositioning, is a strategic approach in pharmaceutical research aimed at discovering new therapeutic applications for existing medications. This study assesses the *in vitro* efficacy of 3-hydrazinoquinoxaline-2-thiol (3HTQ) against *P. aeruginosa*, following promising results with quinoxaline derivatives on other bacterial strains. Broth microdilution-assay was utilised to assess the activity of 3HTQ against 63 different clinical isolates of *P. aeruginosa*. The Minimum Inhibitory Concentrations (MICs) of the tested antibiotic were determined for 63 isolates of *P. aeruginosa*. The MIC levels ranged from 8 µg/mL to 128 µg/mL, whereas the majority isolates (n=32, 50.8%) were at 64 µg/mL, highlighting diverse antibiotic susceptibility among *P. aeruginosa* isolates. Furthermore, we noticed that sixteen isolates (25.4%) and twelve isolates (19%) demonstrated an MIC of 32 µg/mL and 128 µg/mL respectively. Notably, three isolates (4.8%) displayed an MIC of 8 µg/mL, reflecting the highest level of susceptibility among the tested isolates. These findings enforce the requirement of further tests of the genetic variability of these strains with high MIC values to comprehend the resistance mechanisms and their virulence determinants. Further mechanistic studies are required to elucidate the reasons behind these variations in susceptibility. Moreover, exploring the potential of 3HTQ in combination therapies could enhance its overall antimicrobial activity.

Key words: *Pseudomonas aeruginosa*, Repurposing, 3-hydrazinoquinoxaline-2-thiol, Antimicrobial resistance, Gram-negative bacteria.

Bahrain Med Bull 2025; 47 (1): 2763-2770

-
- * Department of Clinical Microbiology and Immunology, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia. aegmusa@kau.edu.sa; kaibrahem@kau.edu.sa; Bhsaleh@kau.edu.sa; tekhmimi@kau.edu.sa; maaalqarni3@kau.edu.sa; nhelmi@kau.edu.sa; hniyazi@kau.edu.sa; hneiazi@kau.edu.sa
- ** Department of Clinical Microbiology Laboratory, King Abdulaziz University Hospital, Jeddah 21589, Saudi Arabia jmokhtar@kau.edu.sa; Dr.dalia2007@hotmail.com
- *** Department of Clinical Biochemistry, Faculty of Medicine, King Abdulaziz University Jeddah 21589 Saudi Arabia. hmdaghistani@kau.edu.sa; yalmoghribi@kau.edu.sa
- **** Department of Medical Laboratory Sciences, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah 21589, Saudi Arabia, walhazmi@kau.edu.sa
- ***** Department of Medical Education, Faculty of Medicine, King Abdulaziz University, Jeddah 21589, Saudi Arabia mabismail@kau.edu.sa
- ***** Department of Microbiology and Parasitology, Faculty of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia osharbi@uqu.edu.sa
- ***** Vaccines and Immunotherapy Unit, King Fahd Medical Research Center, King Abdulaziz University, Jeddah 21589, Saudi Arabia kalkuwaity@kau.edu.sa
- ***** Regenerative Medicine Unit, King Fahd Medical Research Center, King Abdulaziz University, Jeddah 21589, Saudi Arabia ammsait@kau.edu.sa
- ***** Special Infectious Agents Unit BSL-3, King Fahd Medical Research Center, King Abdulaziz University, Jeddah, Saudi Arabia mmufrih@kau.edu.sa
- ***** Centre of Research Excellence for Drug Research and Pharmaceutical Industries, King Abdulaziz University, Jeddah, Saudi Arabia