

Synthesis of novel 2,3-dihydroquinazolin-4(1*H*)-one derivatives and determining their antimicrobial activity via *in-silico* and *in-vitro* study

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The rising antibiotic resistance highlights the crucial need for novel therapeutic agents with improved efficacy. In this study, five novel 6-bromo-2-aryl-2,3-dihydroquinazolin-4(1*H*)-one derivatives bearing various para-substituted phenyl groups, including hydroxy(-OH), nitro (-NO₂), chloro (-Cl) and methoxy (-OCH₃) were synthesized *via* acid-catalyzed cyclocondensation of 2-amino-5-bromobenzamide with corresponding aldehydes, resulting in moderate to good yields (23-66%). The structures of the compounds were confirmed by FT-IR, ¹H-NMR, ¹³C NMR, and HRMS data. Antimicrobial activity of the compounds was evaluated using the standard Agar Well Diffusion assay against *Escherichia coli*, *Proteus mirabilis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Aspergillus niger*. Among the synthesized compounds, the para-hydroxyphenyl substituted derivative exhibited selective antibacterial activity against *S. aureus* across 10.00 and 5.00 mg mL⁻¹ with inhibition zones ranging from 1.2 ± 0.2 to 2.0 ± 0.2 cm, whereas the para-nitrophenyl substituted derivative showed antifungal activity against *A. niger* across 20.00, 10.00, and 5.00 mg mL⁻¹ with inhibition zones

ranging from 2.4 ± 0.0 and 2.9 ± 0.1 cm. The *in silico* molecular docking study targeting proteins, *E. coli* DNA Gyrase and *S. aureus* Sortase A, indicated strong binding affinities (≤ -7.0 kcal/mol) for all synthesized compounds, while the para-nitrophenyl substituted derivative exhibiting binding affinities exceeding -8.0 kcal/mol. All ligands formed stable hydrogen bonds and π-π interactions within the active site and other binding sites, predicting docking efficiencies greater than that of the standard gentamicin and fluconazole drugs. Despite the limited *in vitro* activity observed, which can be attributed to inadequate water solubility and restricted diffusion, combined experimental and computational results emphasize the dihydroquinazolinone scaffold as a promising lead for antimicrobial drug discovery, highlighting the influence of electron-donating and electron-withdrawing substituents on antimicrobial selectivity.

Keywords:

Dihydroquinazolinone, synthesis, antimicrobial activity, in-silico