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ABSTRACT BOOK

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Synthesis of innovative fluoroquinolone analogues as a practical tool for overcoming antibiotic resistance of pathogenic microorganisms

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Background: Resistance to antibiotics has been growing since their introduction into clinical practice [1]. The process of new medicines creation in this area remains parallel to the ability of pathogenic microorganisms to protect themselves and attack humans. Even so, the existing antibiotics can be functionalized to make them more potent and unrecognizable by bacteria. This is the case of fluoroquinolones (FQs) [2-5], which are suitable for various chemical modifications, being a solid base with well-known antibacterial action.

Aims: To synthesize a range of new C-3 modified FQ derivatives based on the results of the docking studies. To determine the structure and purity of the compounds obtained.

Methods: The methods of molecular docking and organic synthesis were used. The molecular structures of the compounds were determined using ^{1}H NMR, ^{13}C NMR, LC/MS spectroscopy and X-Ray diffraction studies.

Results: Docking studies against targets PDB ID: 2XCR and 4KPF identified several promising candidates for combating Gram-positive pathogens. Based on these results, specific structural motifs were identified as key drivers of potential activity, namely: the presence of a fluorine atom at the C-6, the incorporation of a phenylsulfonyl residue into the quinoline core at C-3, and the addition of both electron-donor and electron-acceptor substituents on the phenylsulfonyl fragment. Guided by these insights, a series of 1-substituted 7-(R2',R2''-amino)-6-fluoro-3-(arylsulfonyl)quinolin-4(1*H*)-ones was synthesized. These novel compounds were obtained in moderate yields, with their chemical structure confirmed using modern instrumental analysis.

Conclusion: Docking studies identified several high-affinity candidates among novel 1-substituted 7-(R2',R2''-amino)-6-fluoro-3-(arylsulfonyl)quinolin-4(1*H*)-ones targeting Gram-positive pathogens, specifically Staphylococcus aureus and Streptococcus pneumoniae. A streamlined three-step synthetic route was developed. The compounds were provided for the antibacterial activity testing.

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