2019, Article number e1900086

Synthesis, antibacterial evaluation, and DNA gyrase inhibition profile of some new quinoline hybrids

Rizk, O.H.[a,b]Email Author, Bekhit, M.G.[b], Hazzaa, A.A.B.[a], El-Khawass, E.-S.M.[a], Abdelwahab, I.A.[c]

[a] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Alexandria, Alexandria, Egypt

[b] Department of Pharmaceutical Chemistry, Faculty of Pharmacy & Drug Manufacturing, Pharos University in Alexandria, Alexandria, Egypt

[c] Department of Microbiology and Immunology, Faculty of Pharmacy & Drug Manufacturing, Pharos University in Alexandria, Alexandria, Egypt

Abstract:

Antibiotic-resistant bacteria continue to play an important role in human health and disease. Inventive strategies are necessary to develop new therapeutic leads to challenge drug-resistance problems. From this perception, new quinoline hybrids bearing bioactive pharmacophores were synthesized. The newly synthesized compounds were evaluated for their in vitro antibacterial activity against nine bacterial pathogenic strains. The results revealed that most compounds exhibited good antibacterial activities. Seven compounds (2b, 3b, 4, 6, 8b, and 9c,d) displayed enhanced activity against methicillin-resistant Staphylococcus aureus compared to ampicillin. These compounds were subjected to an in vitro S. aureus DNA gyrase ATPase inhibition study, which revealed that compounds 8b, 9c, and 9d showed the highest inhibitory activity with IC50 values of 1.89, 2.73, and 2.14 μM, respectively, comparable to novobiocin (IC50, 1.636 μM). Compounds 2a–c, 3a, 7c, 9c,d, and 10a,b revealed half the potency of levofloxacin in inhibiting the growth of Pseudomonas aeruginosa. As an attempt to rationalize the observed antibacterial activity for the most active compounds 8b, 9c, and 9d, molecular docking in the ATP binding site of S. aureus gyrase B was performed using Glide. Such compounds could be considered as promising scaffolds for the development of new potent antibacterial agents. © 2019 Deutsche Pharmazeutische Gesellschaft

Reference:

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