Synthesis, Antibacterial Activities, and Synergistic Effects of Novel Juglone and Naphthazarin Derivatives Against Clinical Methicillin-Resistant Staphylococcus aureus Strains

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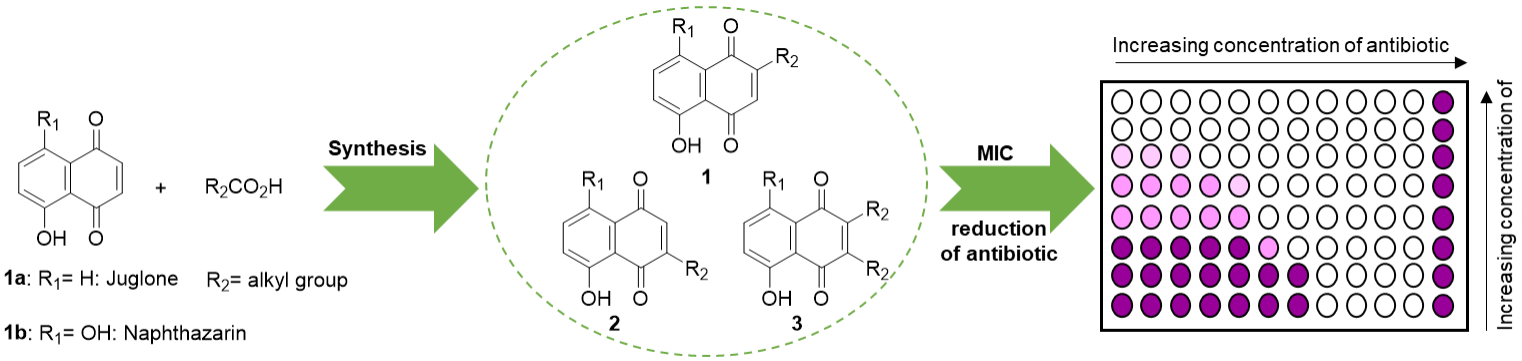
New antibiotics are necessary to treat microbial pathogens, especially ESKAPE pathogens that are becoming increasingly resistant to available treatment[1]. Despite the medical need, the number of newly approved drugs continues to decline[2]. 1,4-Naphthoquinones are known to exhibit an interesting antibacterial activity for instance juglone and naphthazarin, and are a promising new class of compound that can be used to treat bacterial infections. A novel series of 43 juglone/naphthazarin derivatives were synthesized using Minisci-type direct C–H alkylation and evaluated for their antibacterial properties against various clinical and reference Gram-positive *MSSA*, clinical Gram-positive *MRSA*[3]. Different compounds of the synthesized series showed promising activity against clinical and reference MSSA (MIC: 1–8 µg/ml) and good efficacy against clinical MRSA (MIC: 2–8 µg/ml) strains. The synergistic effects of active compounds were evaluated with reference antibiotics (vancomycin and cloxacillin), and it was found that the antibiotic combination with those active compounds efficiently enhanced the antimicrobial activity and consequently the MIC values of reference antibiotics were lowered up to 1/16th of the original MIC. These synthesized compounds did not present hemolytic activity on sheep red blood cells. In addition to the *in silico* prediction of ADME profile parameter which is promising and encouraging for further development.



juglone/naphthazarin derivatives (43 compounds)

References

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