






## Abstract

# Fumiquinazoline-Related Alkaloids with Antibacterial, Anti-Biofilm and Efflux Pump Inhibition Properties <sup>†</sup>

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**Abstract:** With antimicrobial resistance reaching critical levels worldwide, the development of new compounds that are effective against resistant bacterial pathogens or that can potentiate the effect of known antibiotics is an urgent need. The formation of biofilms and the overexpression of efflux pumps are some of the most common causes of drug resistance. Previous work from our group has shown that alkaloids related to the fumiquinazolines have antibacterial potential. Herein we aimed to synthesize a small library of fumiquinazoline-related alkaloids and to study their antibacterial and anti-biofilm activities as well as their capacity to inhibit bacterial efflux pumps. To achieve these goals, two naturally occurring alkaloids, as well as several new derivatives, were synthesized through a multi-step synthetic pathway. The screening of their antibacterial activities was achieved by determination of the minimum inhibitory concentration of each compound against a panel of clinically relevant bacterial species. Several compounds exhibited promising activities against Gram-positive bacteria. Then, using the ethidium bromide accumulation assay, it was possible to identify some compounds with capacity to inhibit efflux pumps. Some of the synthesized alkaloids also showed anti-biofilm potential, reinforcing the idea that fumiquinazoline-related alkaloids can constitute a key strategy for fighting antimicrobial resistance.

**Keywords:** fumiquinazolines; antibacterial; anti-biofilm; efflux pump inhibition



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