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Extended Abstract

Novel Sortase A Inhibitors to Counteract Gram-Positive Bacterial Biofilms †

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Sortase A (SrtA) is a membrane enzyme responsible for the covalent anchoring of surface proteins on the cell wall of Gram-positive bacteria. Nowadays, it is considered an interesting target for the development of new anti-infective drugs which aim to interfere with important Gram-positive virulence mechanisms. Along the years, we studied the anti-staphylococcal and anti-biofilm activity of some natural and synthetic polyhalogenated pyrrolic compounds, called pyrrolomycins. Some of them were active on Gram-positive pathogens at a μg/mL range of concentration (1.5–0.045 μg/mL) and showed a biofilm inhibition in the range of 50–80% [1–3].

We designed and synthesized novel pyrrolomycins, applying an efficient and easy-to-use microwave synthetic methodology. All compounds showed a good inhibitory activity toward SrtA, in accordance with the molecular modelling studies, having IC_{50} values ranging from 130 to 300 μM comparable to berberine hydrochloride. The best compound exhibits a high capability to interfere with biofilm formation of *S. aureus* with an IC_{50} in the nanomolar range. It is also effective in altering *S. aureus* murein hydrolase activity, responsible for degradation, turnover, and maturation of bacterial peptidoglycan [4]. In light of these encouraging results, herein we present our efforts in finding new effective agents able to inhibit biofilm formation.

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