**A multifunctional peptidomimetic macromolecule to fight polymicrobial infections**

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A small number of therapeutic options can at the same time address *Staphylococcus aureus* and *Pseudomonas aeruginosa*, two of the most relevant antibiotic-resistant microorganisms responsible for some polymicrobial infections related to the growth as biofilms and whose damaging effect is well-known.

The design and synthesis of polymers with intrinsic antimicrobial activity have acquired increasing attention as a strategy to treat multidrug-resistant pathogens. In this study, we designed and synthesized a new polymeric derivative (PAA-VC) with glyco-polypeptide architecture bearing L-arginine, vancomycin and colistin as side chains, with the aim to obtain a broad spectrum antimicrobial macromolecule targeting the bacterial surface layers.

PAA-VC has been tested against planktonic forms and established biofilms of reference strains *S.aureus* ATCC 25923 and *P.aeruginosa* ATCC 15442 and susceptible or antibiotic resistant clinical isolates of the above mentioned pathogens. MIC values ranges observed for the conjugate (48 – 190 and 95 – 190 nM for *P. aeruginosa* and *S. aureus* strains respectively) showed higher efficacy if compared with the free vancomycin (MICs within 1.07 – 4.28 μM) and colistin (MICs within 0.63 – 1.33 μM) against planktonic form of tested pathogens. Additionally, being highly biocompatible (IC50 > 1000, 430 and 250 μg/ml for PAA-VC, vancomycin and colistin respectively) high-dosage can be adopted for the eradication of infections in patients. This positively influence the antibiofilm activity on the conjugate leading to a quasi-total eradication of established clinically relevant biofilms (inhibition > 90% at 500 μg/ml).

We believe that the in vitro presented data, especially the antibiofilm activity against established biofilms of two relevant pathogens, the good biocompatibility and the high therapeutic index, might allow the development of PAA-VC as broad spectrum macromolecule to successfully tackle polymicrobial infections.



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