Hybrid multi-tasking peptides and their ionic liquid conjugates as promising leads to tackle severe skin and soft tissue infections

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¶Ana Gomes,[1] Lucinda Bessa,[1#] Iva Fernandes,[1] Nuno Mateus,[1] Paula Gameiro,[1] Ricardo Ferraz,[1,2] Cátia Teixeira,[1] and Paula Gomes[1]

[1] LAQV-REQUIMTE, Departamento de Química e Bioquímica, Faculdade de Ciências, Universidade do Porto, P-4169-007 Porto, Portugal. pgomes@fc.up.pt; [2] Ciências Químicas e das Biomoléculas, Escola Superior de Saúde, Politécnico do Porto, P-4200-072 Porto, Portugal

Polymicrobial biofilms are the most difficult barrier to the treat1ment of complicated skin and soft tissue infections (cSSTI), by being refractory to both the immune system and most current antibiotics, which in turn leads to a chronic state of impaired healing. One case is that of diabetic foot ulcers (DFU), which convey a very poor quality of life for the affected patients and are an increasing burden to healthcare facilities worldwide.[1]The severity of DFU and of other ulcerating cSSTI is not only associated to polymicrobial infections, but also to increased levels of matrix metalloproteinases in the wound bed, which degrade extracellular matrix components such as, e.g., elastin or collagen. Excessive degradation of these and other components further deters the fast and correct healing of these severe wounds, contributing to their chronicity.[2]

Considering the widely demonstrated relevance of host defense peptides (HDP) to fight against multidrug resistant (MDR) microbial pathogens,[3] and the reported collagenesis-boosting action of many small peptides used in the cosmetics industry, such as pentapeptide-4 (PP4),[4] we recently investigated if combination of these two types of peptides could deliver hybrid constructs able to concomitantly display antimicrobial, anti-biofilm, and collagenesis-boosting action. Peptide hybrids were thus produced that exhibited the anticipated multiple action *in vitro*, hence representing promising leads to tackle DFU and other cSSTI.[5,6] Interestingly, *N*-terminal modification of these hybrids by chemoselective conjugation to imidazolium-based ionic liquids (IL) afforded new derivatives that retained the multiple action of the parent peptide.[6,7] Given the foreseen benefits of IL for diverse pharmaceutical applications, including as skin permeation enhancers, these promising results will be highlighted.

References

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[#] Current affiliation: CiiEM - Egas Moniz-Cooperativa de Ensino Superior, CRL, P-2829-511 Almada, Portugal