Common structural motifs in new natural cyclic pentapeptides determine selective antibacterial activity against *Acinetobacter baumannii*

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Aim: As part as our continued efforts for discovering new antibacterial natural products from microorganisms, we have analyzed different *Streptomyces* strains from MEDINA´s microbial collection, for their secondary metabolite production.

Methods: The wide spread increase of bacterial resistance towards conventional antibiotics encourages the exploration of novel antimicrobial molecules with unexploited mechanisms. Among these resistant pathogens, *Acinetobacter baumannii* has proven to be an increasingly important and demanding species in health care–associated infections [1].
The genus *Streptomyces* is known to be one of the most prolific sources of natural products, and it has been estimated to produce over two-thirds of the clinically useful antibiotics of natural origin [2]. Thus, it is definitely worth screening *Streptomyces* strains from different habitats for antimicrobial activity to identify new strains that produce novel antibiotics active against drug-resistant pathogens.

Results: As result of this work, a family of new cyclic pentapeptides with selective activity against *A. baumannii* has been isolated and characterized structurally. The sequences of these cyclic peptides have been established on the basis of their MS/MS fragmentation and 2D-NMR spectroscopic data. These new peptides contain in their structures uncommon amino acids such as N^{δ}-Hydroxy-L-arginine, a naturally occurring but rare amino acid with antibacterial activity itself [3] and also present as substructure in very few siderophore-type and nucleoside antibiotics [4]. To the best of our knowledge, this new family of natural products represents the first class of cyclic pentapeptides containing this residue.

Discussion: Bioactivities of the different members of this new family were evaluated against Gram-negative bacteria such as *A. baumannii, Pseudomonas aeruginosa, Escherichia coli and Klebsiella pneumoniae*. Some of them displayed selective antibacterial activity against a clinical isolate of *A. baumannii.* Core tetrapeptide sequence Leu-Val-Trp-(N^{δ}-Hydroxy-arginine) seems to be essential for retention of the bioactivity / selectivity against *A. baumannii.*

References:

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