Researchers develop a new family of bioinspired antibiotic compounds

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A group of researchers, led by Francesc Rabanal, professor in the Department of Organic Chemistry of the University of Barcelona (UB), has published the first results of a study of a new antibacterial compound based on natural peptides capable of selectively killing resistant pathogens. The study has proved that these compounds are highly active against clinically relevant Gram-negative and Gram-positive bacteria. In vitro and in vivo tests have showed compounds' low toxicity.

Bacterial resistance to almost all available antibiotics is an important public health issue. Moreover, the development of effective antibiotics has slowed down. Only seven new antibiotics were approved by the Food and Drug Administration (FDA) from 2003 to 2012 (only two new classes since 1998). All this makes it clear that there is an urgent need to develop new antibiotics against bacteria that are prone to acquire resistance to the antibiotics currently in use, particularly Gram-negative bacteria. To give an example, more people die in USA of methicillin-resistant Staphylococcus aureus than of AIDS.

"The main goal of the study has been to design, synthetize and prove in vitro activity and in vivo toxicity of a new series of polymyxin, which present potential advantages over currently existing antibiotics", explains Francesc Rabanal, member of the European consortium ENABLE. "One of these advantages is that these antibiotics can act against Gram-negative bacteria, including resistant and multi-resistant strains, which are the most dangerous from the point of view of public health; in addition, they show activity against S. aureus (Gram-positive bacteria)",

concludes the UB researcher.

The institutions who have participated in the project are the Faculty of Chemistry, the Faculty of Pharmacy and the Centre of Research in Toxicology (CERETOX), in the case of the University of Barcelona, as well as the Barcelona Institute for Global Health (CRESIB-ISGlobal) and the Hospital Clínic de Barcelona.

Bioinspired compounds

New compounds designed by Catalan researchers are inspired by cyclic natural antimicrobial peptides (AMPs), particularly polymyxins, a polypeptide antibiotic produced by a Bacillus polymyxa strain which shows some toxicity problems even if it is used as last resort option at hospitals. Design has included a disulphide bond in polymyxin structure which facilitates large-scale synthesis and reduces toxicity.

"The main objective of the study was to design cyclic lipopeptides with a chemically accessible structure, high activity and low toxicity", emphasizes Rabanal. "The next step is to optimise this prototype compound (named hit in the field of pharmacy) in order to obtain a therapeutic candidate (lead) that could be developed in clinical trials and get the market", concludes the researcher.

More information: "A bioinspired peptide scaffold with high antibiotic activity and low in vivo toxicity". *Scientific Reports*, May 2015.DOI: 10.1038/srep10558

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