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Lipophosphonoxins

https://www.iocbtech.cz/project/lipophosphonoxins-2-2/

A NOVEL CLASS OF ANTIMICROBIAL COMPOUNDS WITH A RAPID MECHANISM OF ACTION AND LOW PROPENSITY FOR RESISTANCE DEVELOPMENT

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Novel Broad-Spectrum Antimicrobial Agents to overcome bacterial resistance

CHALLENGE

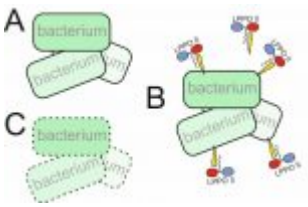
Growing antimicrobial resistance poses a significant threat to public health worldwide. A recent review of the antibiotic pipeline by the World Health Organization (WHO, 17th January 2020) states that the majority of the current drug candidates may have limited benefits compared to already marketed drugs. Innovative solutions are urgently needed.

TECHNOLOGY

Lipophosphonoxins (LPPOs) are novel broad-spectrum antimicrobials with a rapid mechanism of action and low propensity for resistance development. LPPOs selectively target the bacterial membrane of a broad spectrum of clinically relevant Gram-positive and Gram-negative pathogens, including resistant strains (Fig. 1), without damaging eukaryotic cell membranes. As the compounds do not absorb through the gastrointestinal tract, they are intended for topical treatment (for example, in skin infections – Fig. 2).

Antibiotic-resistant infections of the skin and soft tissues are common and may complicate wound healing, e.g., in patients with diabetic ulcers or burn injuries. To address this problem, nanofibrous material with controlled release of LPPOs is currently being

developed in collaboration with Charles University in Prague and the Technical University of Liberec.



LPOO II	Pseudomonas aeruginosa CCM 3955	Staphylococcus aureus MRSA 4591	Staphylococcus haemolyticus 15268	Salmonella ENTERITIDIS S2-25
	MIC [mg/L]			
4c	0.78	6.25	1.56	3.12
4d	3.12	1.56	3.12	6.25
8c	0.78	3.12	1.56	1.56

Figure 1. A schematic illustration of LPPO action and MIC values of selected LPPO against several clinically relevant bacterial strains including resistant ones.

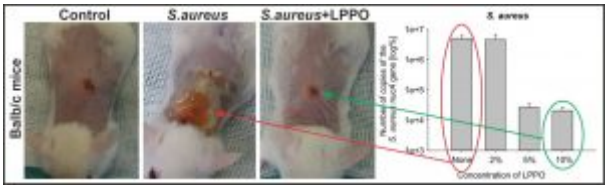


Figure 2. Efficacy of LPPOs against skin infection caused by S. aureus in a mouse model. The photos show uninfected (Control) and Staphylococcus aureus-infected wounds that were either untreated (S.aureus) or NANO-LPPO treated (S.aureus+LPPO). The graph shows the number of remaining bacteria as determined by qPCR.

COMMERCIAL OPPORTUNITY

This project is offered for licensing/collaboration/co-development.

DEVELOPMENT STATUS

The project is in the preclinical/lead optimization phase.

PATENT SITUATION

EP 2 527 351 B1, 11.12.2013, 2013; WO2017186200A1; Czech patent application for the latest generation of compounds – Dec 2019 (PV 2019-769), nanoLPPO

FURTHER READING

1) Seydlová G(1), Pohl R(2), Zborníková E(2)(3), Ehn M(2), imák O(2), Panova N(4), Kolá M(5), Bogdanová K(5), Ve e ová R(5), Fi er R(1), anderová H(4), Vítovská D(4), Sudzinová P(1)(4), Pospí il J(1)(4), Benada O(4), K í ek T(3), Sedlák D(6), Bart n k P(6), Krásný L(4), Rejman D(2). **Lipophosphonoxins II: Design, Synthesis, and Properties of Novel Broad Spectrum Antibacterial Agents.** J Med Chem. 2017 Jul 27;60(14):6098-6118. doi:

10.1021/acs.jmedchem.7b00355. Epub 2017 Jul 12.

2) Rejman D(1), Rabatinová A, Pombinho AR, Kovaříková S, Pohl R, Zborníková E, Kolář M, Bogdanová K, Nyč O, Sanderová H, Látal T, Bartůněk P, Krásný L. **Lipophosphonoxins: new modular molecular structures with significant antibacterial properties.** J Med Chem. 2011 Nov 24;54(22):7884-98. doi: 10.1021/jm2009343. Epub 2011 Nov 1.