**Antimicrobial activity of a chelatable cyclic lipopeptide amphisin produced by* Pseudomonas fluorescens *DSS73**

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Lipopeptides constitute a structurally diverse group of metabolites produced by various bacterial and fungal genera via non-ribosomal pathways [1]. Structurally they are amphiphilic molecules that comprise both hydrophobic and hydrophilic moieties, being the apolar component usually a alkyl chain, whereas the polar part, more variable, can be ion (anionic or cationic) or non-ionic. In the past decades, research on lipopeptides has been focused on their antimicrobial, antitumor and surfactant activities. Amphisin is a lipopeptide with a N-terminal \( \beta \)-hydroxydecanoyl fatty acid side chain and a nonapeptide lactone core resulting from the cyclization of the Thr-3 hydroxyl group onto the C-terminal carboxylate [2].

In the present study, the antimicrobial activity of amphisin obtained by cultivation of *Pseudomonas fluorescens* DSS73 was investigated against multidrug-resistant microorganism such as *Escherichia coli*, *Enterococcus faecalis*, *Staphylococcus epidermidis*, *Proteus mirabilis* and *Candida albicans* found in gastrointestinal and urinary tracts. Amphisin antimicrobial activity was tested in presence or absence of metal ions. The results demonstrated that amphisin in the presence or absence of metal ions has a broad spectrum of action, including antimicrobial activity against microorganisms with multidrug-resistant profiles. Binding to amphisin of Cu\(^{2+}\) and Zn\(^{2+}\) ions increase the antimicrobial activity against *E. coli* and *E. faecalis*. The interaction of lipopeptide with bilayer of bacterial membranes may be facilitated by metal ions, both by neutralizing the anionic charges and by favoring association with the membrane head groups. The results obtained suggest the possible use of this biosurfactant as an alternative antimicrobial agent in the medical field for applications against microorganisms responsible for diseases and infections, making it a suitable alternative to conventional antibiotics. This work was financially supported by grant from the University of Wroclaw No 2319/M-WB/14.

**Keywords:** biosurfactant; *Pseudomonas fluorescens*; lipopeptides; antimicrobial activity

**References**


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**Antimicrobial combination therapies: a network perspective**

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The growing number of resistant strains and biofilm-related infections emerging in healthcare settings and in the general community is a major biomedical concern. Currently, antimicrobial studies are revisiting the potential of old products and looking for new products with alternative modes of action. Most notably, antimicrobial peptides (AMPs) are receiving a lot of attention because of the widespread availability, multiple mechanisms of action, non-specific molecular targets, and anti-biofilm capabilities [1], [2].

Considering that most of the results obtained in these studies lie in scientific literature, and manual curation is time and resource consuming, the development of bioinformatics approaches for the systematic screening of the literature is of obvious interest. In particular, the reconstruction of drug interaction networks reflecting in vitro and in vivo results is considered useful to identify the most promising candidates for the development of alternative antimicrobial therapies, such as antimicrobial combinations [3], [4]. Such networks can aid in profiling and interpreting the activity of AMPs and the added value of antimicrobial combinations, and thus, help exploit their potential.

As a first contribution to this line of analysis, this work presents a novel network reconstruction for results obtained by AMP-drug combinations in fighting *Pseudomonas aeruginosa* infections [5]. This network contains information about strains, combination methodologies, mode of growth, compound description (with drug and AMP database cross-linking) and quantification values (MICs, FICs, log reduction, etc.). So far, the network comprises 239 combinations, such that 83 % of the interactions pair an AMP with a non-AMP compound (antibiotics, enzymes, etc.), mainly traditional antibiotics. The majority (82 %) of the studies focused on the use of combinations on planktonic cells, and surprisingly enough, only 3 % of the studies tested the combination in biofilms. Furthermore, the network is dominated by a small number of highly connected nodes, namely the peptides colistin and polymyxin B. These are the products that are more often tested in antimicrobial combinations.

The network is publicly available, and may be further explore using graph-based analysis tools. Hopefully, this will be a valuable resource to the design of new experiments, unveiling different mechanisms of action and helping in the prediction of new combinations.

**Keywords:** antimicrobial peptides (AMPs); *Pseudomonas aeruginosa*; biofilms; network; bioinformatics

**References**


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