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# BOOK OF ABSTRACTS

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# P4.71 - DRUG REPURPOSING FOR IDENTIFICATION OF NEW EFFLUX INHIBITORS AND/OR ANTIBIOFILM AGENTS AGAINST *STAPHYLOCOCCUS AUREUS* AND *STAPHYLOCOCCUS EPIDERMIDIS*

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## ABSTRACT

*Staphylococcus aureus* (SA) and *Staphylococcus epidermidis* (SE) are frequent agents of nosocomial infections. Staphylococcal efflux-mediated resistance and biofilm formation may render such infections resilient to antibiotherapy.

In this work, we used an *in silico* drug repurposing strategy to identify drugs targeting efflux and/or biofilm formation to be assessed, *in vitro*, for their efflux inhibitory and/or antibiofilm activities.

A list of potential targets, comprising all SA and SE membrane transporters and biofilm-associated proteins, was used to interrogate the DrugBank database and compile a list of drugs targeting homologues of these proteins. A subset of candidate drugs was tested in reference and isogenic strains differing in the expression of *norA*, encoding the NorA efflux pump. Candidate drugs (at ¼ their MIC) were assessed for their ability to inhibit efflux, through reduction of MICs of effluxable antimicrobials and ethidium bromide accumulation fluorometry. Drugs showing significant effect [≥ four-fold MIC reduction and/or a Relative Final Fluorescence value (RFF) ≥ 1] were tested for their potential to inhibit biofilm formation using the crystal violet adhesion method.

We identified over 200 drugs that potentially target SA and/or SE membrane transporters or biofilm-associated proteins. From these, we screened 56 drugs, which showed high MICs (>64 mg/L) against the evaluated strains. Nearly 25% of the candidate drugs significantly decreased the MICs of NorA substrates in *norA*-overexpressing strains and showed an RFF ≥ 1, indicative of efflux inhibitory activity. Additionally, eight drugs, including amlodipine and desipramine, diminished biofilm formation in SA and/or SE.

This study reveals approved drugs with dual targets that, in the future, may be included in the fight against antimicrobial-resistant SA and SE infections.

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