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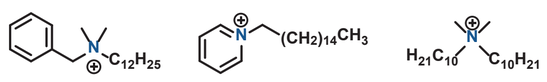
Leveraging novel disinfectants to combat antimicrobial resistance

Disinfectants serve as our first line of defense against pathogenic bacteria. Using a multidisciplinary approach, we are designing new antimicrobial agents with a novel mechanism of action to combat highly-resistant pathogens.

QACs are found in our everyday life





BAC **CPC** **DDAC**

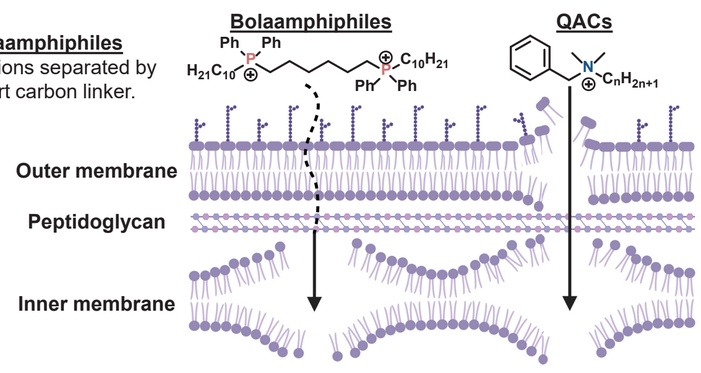
Resistance to QAC disinfectants first reported in the **1980s**.

Overuse and misuse of QAC disinfectants has exacerbated bacterial resistance mechanisms towards these agents.

Carden *et al. ChemMedChem.* **2020**, *15* (21), 1974. Mahoney *et al. iScience.* **2021**, *24* (4).

Bolaamphiphiles selectively target the inner membrane

Bolaamphiphiles
Two cations separated by a short carbon linker.



Will bolaamphiphiles exhibit superior bioactivity compared to QACs against highly resistant clinical isolates?

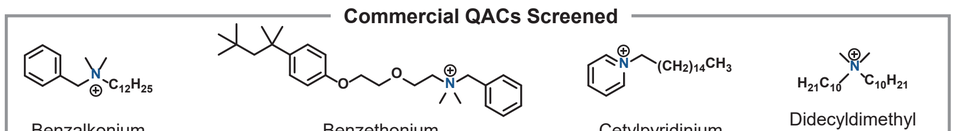
Sanchez, C.A. *et al. ACS Infect. Dis.* **2024**, 10, 3868-3879.

Pseudomonas aeruginosa and Disinfectants



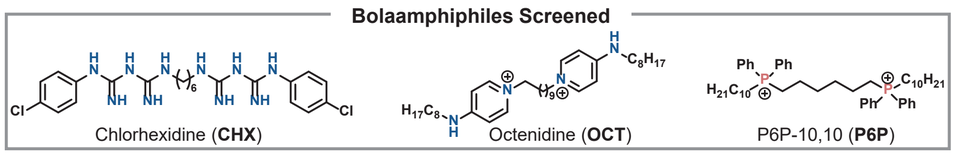
Panel of 50 highly resistant *Pseudomonas aeruginosa* clinical isolates
- Isolated from two facilities in the United States
- Persisted on sink surfaces after treatment with peroxide or QAC-based disinfectants
- Harbor multiple antibiotic and disinfectant resistance genes

Commercial QACs Screened



Benzalkonium chloride (**BAC**) | Benzethonium chloride (**BEC**) | Cetylpyridinium chloride (**CPC**) | Didecyldimethyl ammonium chloride (**DDAC**)

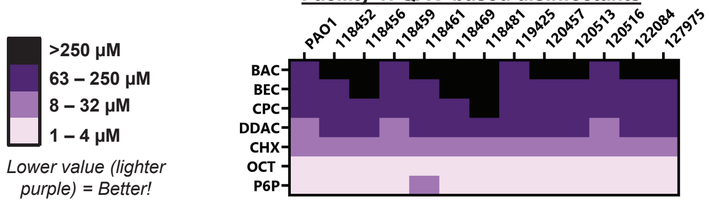
Bolaamphiphiles Screened



Chlorhexidine (**CHX**) | Octenidine (**OCT**) | P6P-10,10 (**P6P**)

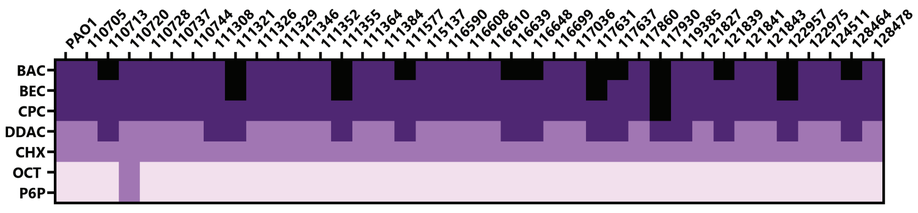
Bolaamphiphiles overcome clinical QAC resistance

Facility 1: QAC-based disinfectants



Lower value (lighter purple) = Better!

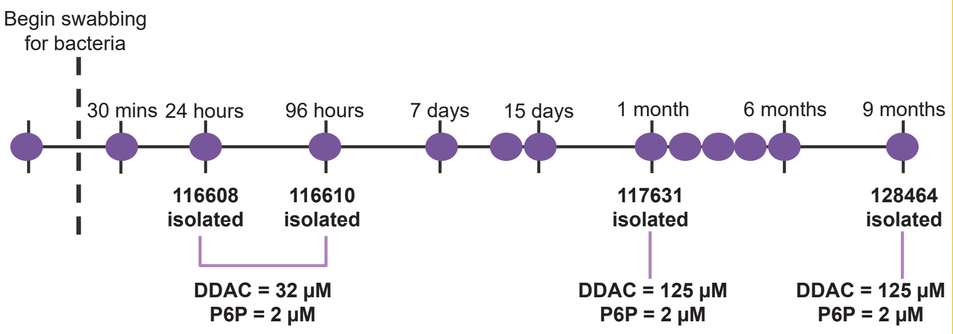
Facility 2: Hydrogen peroxide-based disinfectants



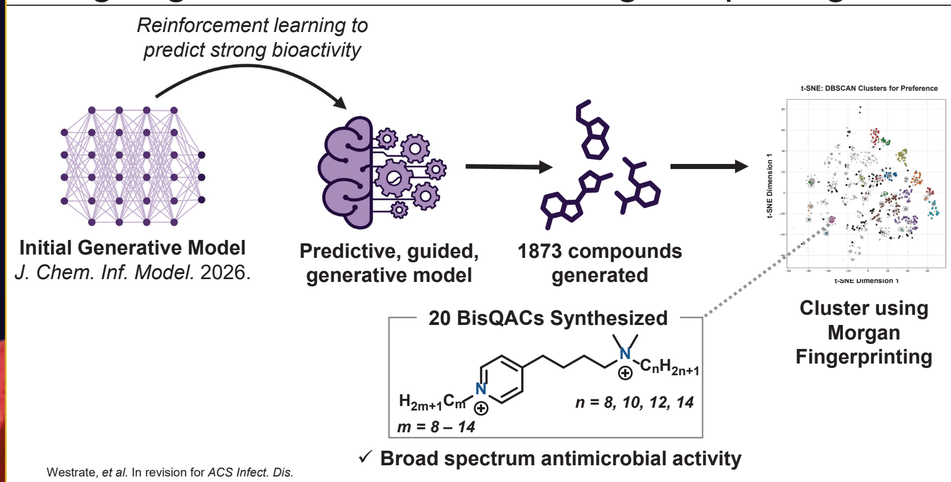
Facility 2: Mapping resistance in real time

= disinfectant treatment

We observed **increasing MICs for DDAC as disinfection continued over time**. In contrast, the **MIC for P6P-10,10 remained stable**, demonstrating its ability to **overcome clinical QAC resistance**.



Designing disinfectants with AI to fight superbugs



Westrate, *et al.* In revision for *ACS Infect. Dis.*

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