Novel adjuvant to re-sensitise antibiotic resistant bacteria for the treatment of pyoderma

KEY FEATURES

- **Pyodermas are common in humans and animals and associated with many multidrug-resistant organisms, diminishing the range of antibiotics available, resulting in clinical need for treatment options**
- **Adjuvants which restore the activity of existing antibiotics against several resistant bacterial strains are in development thus prolonging their use**
- **The adjuvants identified re-sensitised Group A streptococcus (GAS) to tetracycline in a skin infection model**

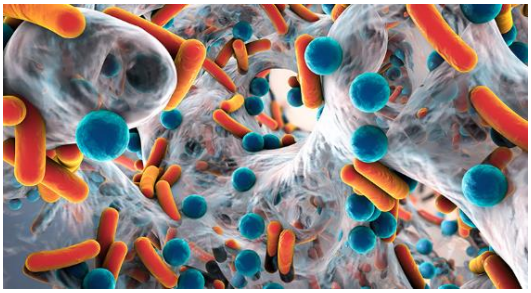
Background

Pyoderma is one of the most common clinical conditions encountered in humans and animals and is typically caused by one of two bacteria: *Staphylococcus aureus* or *Streptococcus pyogenes* (Group A streptococcus). Children and companion animals, dogs in particular, are highly prone to the disease leading to poor health outcomes.

The most common organism isolated in pyoderma is *S. aureus*, which may be either methicillin-sensitive (MSSA) or methicillin-resistant (MRSA). In dogs, the most commonly isolated causal pathogen is *S. pseudintermedius*, however others such as *S. aureus* and *E. coli* have also been identified. Many of these isolates are becoming multidrug resistant. All β-lactams including carbapenems and high-end cephalosporin, piperacillin, tazobactam etc. are ineffective against MRSA.

Market Potential

The market demand for pyoderma medication is significantly high due to its common occurrence and recurrent diagnosis in humans and animals. There is a need for affordable treatment which can cure the disease at a faster rate without causing side effects. Erythromycin has long been a mainstay of pyoderma therapy, but its use is contraindicated in areas in which erythromycin-resistant strains of *S. aureus* or, more recently, *S. pyogenes* are prevalent.



Pyoderma management in the age of methicillin resistance is an ongoing challenge. Many MRSA infections are also multi-drug resistant complicating treatment and limiting therapeutic options. MRSA is an important health care-associated pathogen. In general, higher prescription rates seem to be associated with higher resistance rates. Resistance towards other commonly-prescribed antibiotics to treat pyoderma is therefore of great concern. Consequently, there is a market need for compounds which restore the activity of existing antibiotics against these resistant bacterial strains to address the urgent threat.

Technology

Researchers from The University of Queensland (UQ) have identified adjuvants which can re-sensitise tetracycline-resistant strains of group A streptococcus and restore its activity in a skin infection model (Figure 1).

In figure 1, topical application of adjuvant + Tet reduces the number of viable bacteria compared to Tet or adjuvant alone.

Figure 1: Skin Infection Model – HKU16, GAS strain

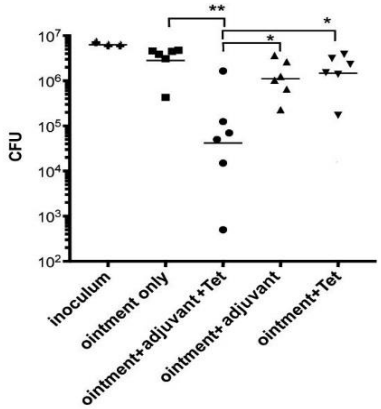


Fig. 1. Modified from Pandey, M., et. al., *J. Immunol.* **194**, 5915-5925 (2015). Mice were tested twice daily for 2 days with 25-30mg ointment applied to the surface of the wound. Tetracycline (Tet) was added to carrier cream to 1.5% where indicated. Mice were sacrificed on day 2 and GAS CFU in infected skin elucidated.

Co-administration of the adjuvant also re-sensitises *Staphylococcus aureus* strain USA300 (Table 1) and GAS (Table 2) to several antibiotics, including Erythromycin and Polymyxin B, commonly used to treat pyoderma. The β-lactams – Oxacillin and Ampicillin that were ineffective against MRSA were also re-sensitised. (Tables 1 & 2).

Table 1. Treatment of MRSA

Antibiotic	MIC (µg/mL)	
	Antibiotic only	Antibiotic + adjuvant
Methicillin*	>128	>128
Oxacillin*	128	1-2*
Erythromycin	64	0.5*
Ampicillin	>128	2*
Polymyxin B	64	2
Colistin	>128	2

* +2 % NaCl as per CLSI guidelines

(Interpretive standards: Resistant, sensitive, intermediate)

Table 2. Treatment of resistant GAS

Antibiotic	MIC (µg/mL)	
	Antibiotic only	Antibiotic + adjuvant
Erythromycin	>128	>128
Tetracycline	64-128	2-4
Polymyxin B	64-128	1-2
Colistin	>128	0.5-1

(Interpretive standards: Resistant, sensitive, intermediate)

*The MIC for different antibiotics was determined by broth microdilution for MRSA (according to CLSI).

Commercialisation Opportunities

We are seeking licensing or collaborative partners with whom we can further develop this technology and demonstrate the clinical efficacy of this work.

References

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3. Koning, S., et. Al., 2004, *BMJ: British Medical Journal*, **329**(7468), 695-696.

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RESEARCH TEAM

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