

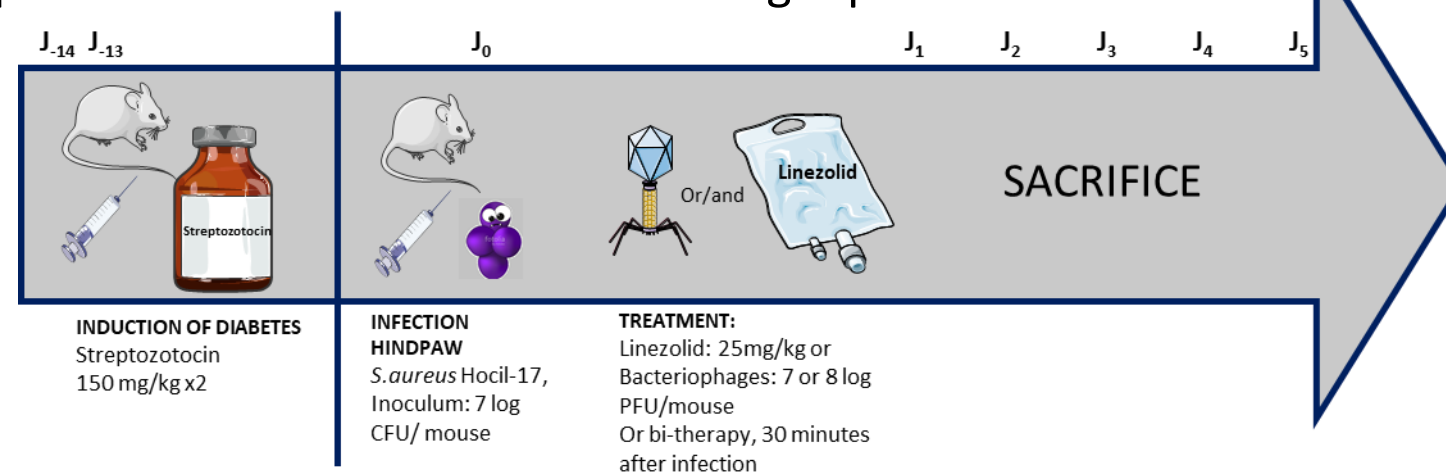
Introduction

DFUs are the most common cause of hospitalization among diabetic patients and *Staphylococcus aureus* is the major pathogen implicated. Antibiotic treatment of DFU is complicated by the formation of heterogeneous biofilms, which involve bacteria resistant/tolerant to antibiotic. Bacteriophages are viruses that target specific bacteria, offering an alternative for the treatment of bacterial infections. In this study, we evaluated the efficacy of a combination of three lytic bacteriophages, in comparison to linezolid, in a mouse model of *S. aureus* DFU infection.

Methods

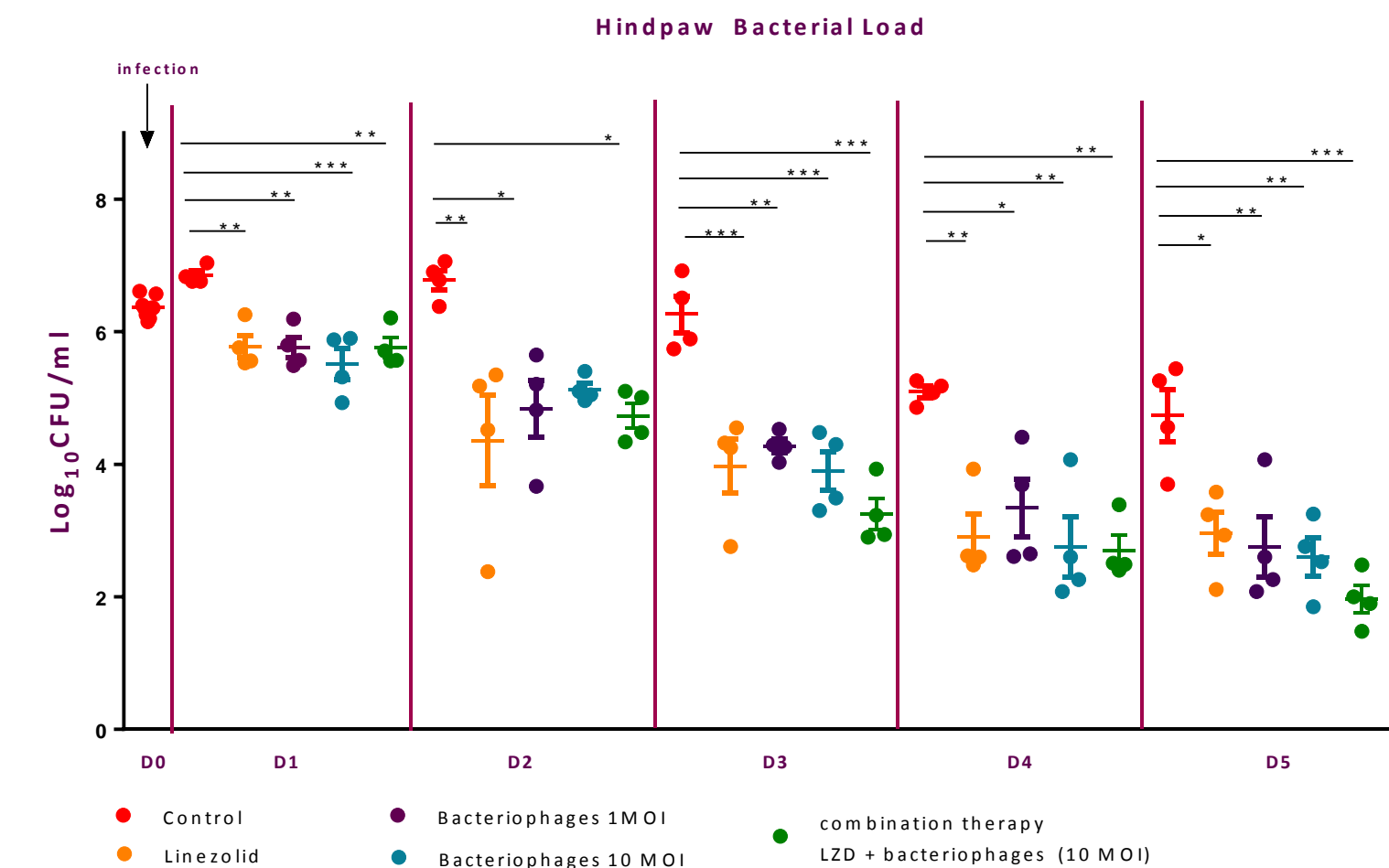
An acute hindpaw infection was established in streptozotocin (150mg/kg x2) induced diabetic BALB/c mice, using a 7 Log₁₀ CFU/mouse inoculum of the MSSA Hoci1-17 clinical strain.

Thirty minutes after infection, mice received an intraperitoneal administration of linezolid (25mg/kg), or a local administration of bacteriophages at two different doses: 1 MOI or 10 MOI (MOI: Multiplicity of Infection) or the association of linezolid and 10 MOI of bacteriophages. Control mice were infected but untreated. Mice from each group were sacrificed on day 0, 1, 2, 3, 4 & 5 and the residual bacterial load in the hindpaw was enumerated on selective agar plates.



Results

- While the bacterial load remained stable in the hindpaw of untreated diabetic animals over the first 3 days post-infection, it slightly decreased after day 4.
- All treatments provided a significant bacterial reduction in the hindpaw over time.
- Interestingly, a single injection of bacteriophages was sufficient to induce the decrease of residual bacterial load in the hindpaw, to a level comparable to linezolid.
- The association between linezolid and bacteriophages resulted in an increased reduction compared to bacteriophages alone at day 5, highlighting the synergy between the two treatments.



Conclusion

The therapeutic efficacy of well-characterized bacteriophages for treating *S. aureus* DFU in mice demonstrated a significant bacterial reduction similar to linezolid, when compared to control animals. This work highlights the efficacy of bacteriophages therapy for *S. aureus* DFU infections, that are one of the leading causes of amputation and morbi-mortality among the diabetic population.

Chhibber *et al.*, PlosOne, 2013; Rich and Lee, Diabetes, 2005; Szkudelski, Physiological Research, 2001.

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